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PSYCHOPHARMACOLOGY ABSTRACTS

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

238738 Koe, B. Kenneth. Central Research Pfizer Inc., Groton, CT 06340 **Conformational requirements for blocking uptake of catecholamines and serotonin into crude rat brain synaptosomes.** Federation Proceedings. 35(3):527, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, conformational requirements for blocking uptake of catecholamines and serotonin (5-HT) into crude rat brain synaptosomes were reported. Several agents of relatively rigid molecular structure have been found to strongly block monoamine uptake by synaptosomal preparations of rat corpus striatum and hypothalamus. These include CP-24,441 (1R,4S-N-methyl-4-phenyl-1,2,3,4-tetrahydro-1-naphthylamine), EXP-561 (4-phenylbicyclo(2,2,2)octan-1-amine), nomifensine, and nefopam. A basic conformational requirement for uptake blocking activity for phenylbutylamine and phenoxypropylamine related inhibitors is that the relative separation and orientation of phenyl and amino groups resemble that of EXP-561. The tubular configuration of EXP-561 may be the most appropriate for blocking 5-HT uptake. The requisite conformation for blocking dopamine uptake appears to be defined by the combination resulting from superimposition of the CP-24,441 and nomifensine structures. The conformation defined by the combination resulting from superimposition of the CP-24,441 and desipramine structures is apparently optimal for blocking NE uptake. (Journal abstract modified)

238762 Van Riper, Dee A.; Hanlon, David P.; Stolk, Jon M. Dept. of Pharmacology, Dartmouth Medical School, Hanover, NH 03755 **Phenylethanolamine-N-methyltransferase: S-methylation of 4-(n-butyl)-imidiazole-2-thiol.** Federation Proceedings. 35(3):486, 1976.

At th 60th annual meeting of the Federation of American Societies for Experimental Biology, a partially purified preparation of the enzyme phenylethanolamine-N-methyltransferase (PNMT) catalyzes the formation of (PNMT) radioactive produced from 4-(n-butyl)-imidazole-2-thiol (4-n-butyl 12T) in the presence of (14C-methyl) s-adenosyl-L-methionine. The radiomethylated product also was formed when PNMT purified to antigenic purity, as evidenced by a single band on SDS electrophoresis, was used as an enzyme source. The site of methylation appears to be on the sulfur atom rather than on either of the two nitrogen atoms. The methylthioether derivative of 4-n-butyl-12T is identical to the radioactive product obtained upon incubation with PNMT, as determined by high pressure liquid chromatography; additionally, the methylthioether derivative is not converted into radioactive product by PNMT. 4-n-Butyl-12T competitively inhibits the formation of N-methyl octopamine by PNMT; octopamine competitively inhibits S-methylation of the 12T derivative. (Journal abstract modified)

238774 Godse, D. D.; Warsh, J. J.; Stancer, H. C. Clarke Institute of Psychiatry, 250 College Street, Toronto, Ontario, Canada M5T 1R8 **Gas-chromatography-mass fragmentographic (GC-MF) analysis of tryptamine in biological samples.** Federation Proceedings. 35(3):523, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a gas chromatographic/mass fragmentographic (GC-ME) analysis of N-acetyl-1-trifluoroacetyl (TRYP-NA-TFA) or N-acetyl-1-pentafluoropropionyl (TRYP-NA-PFP) was presented. After extraction of neutral compounds at acid pH with diethyl ether, tryptamine (TRYP) was acetylated by reaction of urine or deproteinized brain samples at pH 10-10.5with acetic anhydride (1%) delivered in diethyl ether. After evaporation of the ether extractant to dryness under N2, TRYP-NA-TFA was prepared by reaction of the residue with trifluoroacetic anhydride in ethyl acetate (1:5). TRYP-NA-PFP was prepared by reaction with pentafluoropropionic anhydride in ethyl acetate (1:5). GC-MF was performed on a Finnigan 3200 instrument equipped with programmable ion monitors. Mass spectral analysis of TRYP-NA-TFA revealed prominent ions at 183 and 280 amu, while TRYP-NA-PFP had abundant ions at 183 and 330 amu. The assay of TRYP as its TRYP-NA-TFA derivative permitted linear assays of 1 ng sensitivity for urine, while assays of 250 pg sensitivity were achieved in rat brain analyses using the TRYP-NA-PFP derivative. (Journal abstract modified)

238775 Brunswick, David J.; Mendels, J. Affective Diseases Research Unit, VA Hospital, Philadelphia, PA 19104 **Radioimmunoassay of tricyclic antidepressants.** Federation Proceedings. 35(3):531, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a sensitive radioimmunoassay for tricyclic antidepressants was reported. The tricyclic hapten N-succinylnortriptyline was synthesized and rendered immunogenic by coupling to bovine serum albumin using the carbodiimide method. Antisera induced by immunization of rabbits with this tricyclic protein conjugate were tested using 3H-imipramine (3H-IMI) with specific activity about 5 Ci/mmole. The antisera were capable of binding imipramine, amitriptyline (AMI), doxepin, desmethylimipramine and nortriptyline. About 1.5ng unlabeled AMI produced 50% inhibition of 3H-IMI binding. As little as 0.2ng AMI could be measured reliably. The tricyclic compounds in plasma were separated from their major metabolites by extraction of alkaline plasma with n-heptane containing isoamyl alcohol followed by back extraction into acetate buffer. (Journal abstract modified)

238776 Shostak, Michael; Perel, James M. NYS Psychiatric Institute, New York, NY 10032 **Raidoimmunoassay for haloperidol.** Federation Proceedings. 35(3):531, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a radioimmunoassay for haloperidol (Hal) was reported. The minimum detectable amount of drug was 0.2ng. Using 0.1ml of serum added directly to each assay tube, the sensitivity was 2 ng/ml. The metabolites p-fluorophenylacetic acid, beta(p-fluorobenzoyl) propionic acid and p-fluorophenaceturic acid showed no appreciable cross reactivity with the parent drug at 25.0ng. The compound 4-(p-chlorophenyl) 4-hydroxypiperidine, a potential metabolite whose presence has not as yet been demonstrated, showed limited cross reactivity. Five ng resulted in a binding inhibition of 25% (compared with 50% for 1 ng of parent drug). A number of other neuroleptics were tested for cross reactivity. Bromperidol was indistinguishable from (Hal). Chlorpromazine, thioridazine, trifluoperazine and fluphenazine showed no cross-reactivity whatsoever. Sera from patients receiving (Hal) was assayed using this method. 1 reference. (Journal abstract modified)

238818 Forrest, Irene S.; Green, Donald E.; Serra, Mauricio T.; Loeffler, Kay O. VA Hospital, Palo Alto, CA 94304 **Improved assays of chlorpromazine and its metabolites.** Federation Proceedings. 35(3):667, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the methodology for the assay of chlorpromazine (CPZ) and its biotransformation products, such as column and thin layer chromatographies, sequential solvent extractions, enzymatic, alkaline and acid hydrolyses was discussed. The relative quantities of individual CPA metabolites extracted in the various steps were determined by gas chromatography/mass spectrometry (GC/MS) using McLafferty's Probability Based Matching (PBM) algorithm. Only the major and most significant CPZ metabolites were incorporated into the metabolite panel which was evaluated with regard to specificity, sensitivity and saving of time. It appears that the computerized and fully automated PBM procedure is a suitable analytical method for hospital laboratories in which CPZ plasma concentrations or metabolite profiles in blood or urine are to be determined. While sample preparation requiring hydrolyses was not negligible, the PBM analysis as such requires between 5 and 10 min for the entire metabolite panel in which the detection limits for individual CPZ derivatives are in the low nanogram range. (Journal abstract modified)

239659 Zalipsky, J. J.; Patel, D. M.; Darnowski, R. J.; Reavey-Cantwell, N. H. Analytical and Physical Chemistry Dept., Research Division, William H. Rorer, Inc., Fort Washington, PA 19034 **pKA determination of methaqualone.** Journal of Pharmaceutical Sciences. 65(3):460-461, 1976.

The use of an ultraviolet spectrophotometric method to determine the pKA value of methaqualone at two independent analytic wavelengths and in different pH media is described. The protolytic constant thus determined, pKa equal to 2.54, is in agreement with values previously reported by Patel and by Schulman. It is argued that the pKa value of 3.56 obtained by Chatten et al. by potentiometric titration of methaqualone in a varying composition of acetone/water solvent systems is questionable. Unnecessary complications and consequent unreliabilities inherent in the use of such mixed solvent systems are pointed out. 5 references.

239660 Smith, Robert V.; Erhardt, Paul W.; Rusterholz, David B.; Barfknecht, Charles F. Drug Dynamics Institute, College of Pharmacy, University of Texas, Austin, TX 78712 **NMR study of amphetamines using europium shift reagents.** Journal of Pharmaceutical Sciences. 65(3):412-417, 1976.

The enantiomeric compositions of amphetamine and certain of its methoxylated derivatives were assayed using europium nuclear magnetic resonance shift reagents. The stereospecificity of the shifting process was investigated by employing tris(3-trifluoroacetyl)-d-camphorato)europium, a chiral shift reagent, with stereochemically pure enantiomers and known enantiomeric mixtures. Although certain (R)-enantiomers showed greater downfield C-methyl group shifts, these shift differences from the corresponding (S)-enantiomers were small and not well resolved. 48 references. (Author abstract modified)

241350 Mansuy, D.; Beaune, P.; Chottard, J. C.; Bartoli, J. F.; Gans, P. Laboratoire de Chimie de l'Ecole Normale Superieure, CNRS, No. 32, 24, rue Lhomond, 75231, Paris Cedex 05, France **The nature of the "455 nm absorbing complex" formed during the cytochrome P450 dependent oxidative metabolism of amphetamine.** Biochemical Pharmacology (Oxford). 25(5):609-612, 1976.

The active metabolite of amphetamine derived from N-oxidation was identified among the possible intermediates arising with the successive oxidation steps from amphetamine to the nitro derivative. The oxime having the next higher oxidation level after N-hydroxy amphetamine and being the stable tautomer of the nitroso derivative, gave no difference spectra with rat liver microsomes either directly in a reducing medium or after pretreatment by reduced nicotinamide-adenine dinucleotide phosphate (NADPH) and oxygen followed by dithionite reduction. On the contrary, the nitro compound, prepared by oxidation of the oxine by CF3C03H, interacted with rat liver microsomes, in the presence of excess sodium dithionite, leading to the formation of an intense difference spectrum with a peak at 455 nm. Aliphatic nitro compounds also exhibited a strong interaction with other reduced hemo proteins, hemoglobin and myoglobin, but only in the presence of an excess of sodium dithionite. The need of a reducing agent for the formation of the new hemoglobin-A complex indicates that it is not derived from the direct interaction of deoxy-hemoglobin-A with the nitro compound but from its interaction with a metabolite formed by a reduction of the nitro compound with dithionite, either directly or via the hemoglobin-A heme. It is suggested that these preliminary results should lead to a correlation between the structure of some amino or nitro compounds and their ability to produce a 455 nm absorbing cytochrome P450 complex after metabolization. 19 references.

242003 Butterick, John Robert. Simon Fraser University, Canada **Synthesis of "O-transmethylated" catecholamines and psychodysleptic beta-phenylisopropylamines. (Ph.D. dissertation).** Dissertation Abstracts International. Ottawa, National Library of Canada.

Synthesis of O-transmethylated catecholamines and beta-phenylisopropylamines is discussed. Optimized yields from chemical incorporation of 14C-label through specific synthetic routes in the elaboration of ring substituted beta-phenylisopropylamines are reported. Preliminary tolerance/cross-tolerance studies in mice of mescaline and 1-(3,4-dimethoxyphenyl)-2-aminoethane were performed, and results from these studies are reported. Five unreported compounds of the beta-phenylisopropylamine were synthesized. A synthetic route for 14C-side-chain labeling in the series was explored. Optimization of yields, facile condensation conditions, utilization of a new reducing agent, and possible syntheses of general application are described. Application of this series of beta-phenylisopropylamines in psychotherapy is considered. (Journal abstract modified)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

238805 Osgood, Patricia F.; Pars, Harry C. Sharps Associates (SISA), 767 B Concord Avenue, Cambridge, MA 02138 **Structure activity relationships in analogs of delta9-tetrahydrocannabinol: tachycardia vs. analgesia.** Federation Proceedings. 35(3):643, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the structure activity relationships in analogs of delta9-tetrahydrocannabinol (THC) were reported. A series of substituted benzopyrans previously evaluated for their analgesic potency (AP), were tested for their effects on the heartrate of the unanesthetized rat. The THC molecule was modified at one or more of three localizations: the alicyclic ring, the n-amyl side-chain of the aromatic ring, the OH group of the aromatic ring with gamma-substituted butyric acids to form water soluble esters. Esterifica-

tion of THC with a gamma-morpholino butyrate group slightly decreased the tachycardia potency (TP) but did noting to enhance AP. If instead the side chain was changed from n-amyl to 1,2-dimethyl heptyl (C9), TP decreased while AP increased. Esterification of the C9 derivative further reduced TP. Replacing the acyclic ring in the C9 derivative with a heterocyclic ring led to less TP than with THC while AP markedly increased. Esterification of this last compound lowered TP and retained the gain in AP. Modification of this ester with alpha-methyl group again reduced TP with little change in AP. Addition of a 2-methyl group to the piperidine ring of the ester gave the compound of least TP and greatest AP in this series. (Journal abstract modified)

240937 Chuang, Helen Lom-seng. University of Illinois at the Medical Center **Congeners of phenothiazine tranquilizers. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-26170 HC$18.00 MF$7.50 78 p.

Attempts were made to discover congeners of phenothiazine tranquilizers by substituting side-chains at the nitrogen of the tricycle system. A series of chlorpromazine analogs, namely, 10-(alkoxyiminoalkyl)phenothiazines, was synthesized, and two synthetic routes were used for preparing the desired compounds: 1) the condensation of phenothiazine and appropr[illegible] 2-alkoxyiminoalkyl bromides in the presence of sodium hydride, and 2) the reaction of alkoxyamines with 10-(diethoxyethyl)phenothiazine. Problems encountered in these two methods are described, and the compounds were investigated in pharmacological tests for central nervous system (CNS) depressant activity. When tested in mice, all compounds showed an order of activity comparable to that of chlorpromazine. Because 10-((2-hydroxyimino)ethyl)phenothiazine was aciic and less lipophilic than the rest, it was the least potent in CNS depression, as expected. Surprisingly, 10-(1,2-dimethyl-2-methoxyiminoethyl)phenothiazine was more potent than chlorpromazine in animal tests. The remainder of the compounds were 5 to 70 times less active than chlorpromazine in terms of DD50 (mg/kg). An attempt was made to determine the median lethal dose, but no deaths were found at the dose of 1000mg/kg. All compounds showed low toxicity. (Journal abstract modified)

241359 Rauws, A. G.; Olling, M.; Freudenthal, J.; ten Han., M. Laboratory of Pharmacology, National Institute of Public Health, Bilthoven, The Netherlands **Azaperol, a new metabolite of the veterinary butyrophenone tranquilizer azaperone.** Toxicology and Applied Pharmacology. 35(2):333-339, 1976.

After intramusclar injection of the butyrophenone tranquilizer azaperone in pigs, an unknown substance was found at the injection site and in brain, liver and kidney extracts. With the aid of mass spectrometry the substance was identified as a reduction product, the corresponding carbinol derivative. The substance is provisionally named azaperol. The structure was confirmed by synthesis. Although azaperol is more polar than azaperone, it has some neuroleptic activity. After intravenous administration of azaperol to rats, part of it is oxidized to azaperone. 7 references. (Author abstract)

242002 Elliott, Glen Raymond. Stanford University **Tryptolines: pharmacological and enzymological studies. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-5725 HC$18.00 MF$7.50 209 p.

The successful identification of the actual enzymatic products from tryptamine substrates and 5-methyltetrahydrofolate are described and the pharmacological study of 5-hydroxytryptoline is presented. Comparison of the enzymatic products from tryptamine and omega-N-methyltryptamine with authentic N-methylated standards in several thin-layer chromatographic systems conclusively demonstrated that methylation does not occur at either nitrogen. Instead, a previously undescribed enzymatic reaction occurs in which a one-carbon unit is transferred from 5-methyltetrahydrofoiic acid, followed by an intramolecular cyclization to yield the analogous tryptoline. Thus, tryptamine yields tryptoline, omega-N-methyltryptamine yields 1-methyltryptoline, and 5-hydroxytryptamine yields 5-hydroxytryptoline. Enzymatic products were identical to the appropriate tryptoline in each of at least three thin-layer chromatographic systems. Each radioactive product, when mixed with unlabeled authentic standard, yielded a substance with a specific activity which remained constant through successive crystallizations in three different solvent systems. By gas liquid chromatography/mass spectrometry, each product had a retention time and a mass spectrum identical to that of the appropriate tryptoline standard. These results prove that the 5-methyltetrahydrofolate dependent enzymatic preparation is not involved in the N-methylation of tryptamine substrates; thus, this enzyme cannot be involved in the production of such substances in schizophrenics. (Journal abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

238672 Morgan, James P.; Van Maanen, E. F.; Mohammed, S. University of Cincinnati College of Medicine, Cincinnati, OH 45267 **Differential blockade of alpha-adrenergic receptors by chlorpromazine.** Federation Proceedings. 35(3):209, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effect of chlorpromazine (CPZ) on the pressor responses to norepinephrine (NE) and phenylephrine (PE) in the isolated, perfused dog hindlimb was presented. NE is ten times more potent than PE. Similar maximal pressor responses could be obtained with both drugs, and neither drug produced vasodilatation. Dose-response curves to intraarterial NE and PE were performed before and after intravenous CPZ. CPZ had no effect on the pressor responses to either NE or PE. CPZ did not effect the NE responses, but produced a shift in the PE dose response curves. After CPZ, the NE dose response curves were shifted two times to the right; the PE dose response curves were shifted fifteen times to the right. In low doses CPZ competitively antagonized the effects of PE without affecting the NE responses, indicating that these agonists stimulate different alph-adrenergic receptors and that cpz has a ten times greater affinity for one of the receptors. (Journal abstract modified)

238673 Thoa, N. B.; Tizabi, Y.; Maengwyn-Davies, G. D.; Kopin, I. J.; Jacobowitz, D. M. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Catecholamine concentration in discrete areas of brain of several strains of mice: correlation with aggressivity.** Federation Proceedings. 35(3):209, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of norepinephrine (NE) and dopamine (DA) in 14 selected areas of the brains of adult male mice from five strains was presented. A comparison between the most aggressive (Swiss-Webster) (SW) and the most submissive (A/HeJ) strains showed that in the

SW mice NE levels were significantly higher in frontal cortex, nucleus accumbens, caudate nucleus, septal area and dentate gyrus, significantly lower in the medial preoptic nucleus and hypothalamus and, equal in the olfactory tubercle, substantia nigra compacta, prepiriform, cingulate and entorhinal cortices, lateral preoptic nucleus and hippocampus. DA concentrations were higher in the nucleus accumbens, cingulate cortex and hypothalamus. It is concluded that in general amine levels are comparable in brains of mice and rats. In most areas examined, there was no correlation of amine levels with strain aggressivity. (Journal abstract modified)

238674 Kang, Sungzong; Strzelczyk, Marian; Johnson, Carl L.; Green, Jack P. Department of Pharmacology, Mount Sinai School of Medicine, CUNY, New York, NY 10029 **LSD binding in subcellular fractions of rat brain and inhibitory effects of ring-substituted tryptamines.** Federation Proceedings. 35(3):241, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the inhibitory effects of ring substituted tryptamines in rat brain were reported. Lysergic acid diethylamide (LSD) binds stereospecifically and saturably to the subcellular fractions of the rat brain homogenates. Among fractions, the microsomal P3 fraction shows maximum specific binding as well as the highest ratio of specific to nonspecific binding. Treatments of P3 fraction with the membrane destabilizing agents such as phospholipase C, freeze thawing, and vigorous polytronization markedly increase not only the maximum binding but also the ratio of specific to nonspecific binding. Proteolytic enzymes and solubilizing agents such as TX100 and deoxycholate diminish the LSD binding. The IC50 of serotonin varies with degree of fractionations: with P2 fraction the value is 3.6microM; with P3 fraction 2.3microM; with freeze thawed P3 fraction 1.05 microM. (Journal abstract modified)

238675 Tabakoff, Boris; Moses, Frances. Department of Physiology, University of Illinois Medical Center, Chicago, IL 60612 **Differential effects of tranylcypromine and pargyline on indoleamine systems in brain.** Federation Proceedings. 35(3):241, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of tranylcypromine (TCP) and pargyline (Pg) on activity and temperature in mice were reported. TCP increased activity while Pg lowered activity compared to control mice. Temperature was lowered with Pg and unaffected by TCP. Doses of TCP and Pg similarly inhibited monoamine oxidase (MAO), but TCP was found to significantly elevate brain tryptophan (try). The increase in brain try was dose dependent with TCP; Pg had no effect. Increases in brain try after TCP were accompanied by increases in free try in plasma. Although try levels in brain were increased as much as 100% after TCP, no change in the rate of accumulation of serotonin (5-HT) was found between animals treated with Pg or TCP. Results were interpreted on the basis of formation of indoleamines other than 5-HT or direct action of TCP on norepinephrine. (Journal abstract modified)

238676 Hirsch, M. J.; Fernstrom, J. D. MIT, Cambridge, MA 02139 **Stimulation of brain serotonin (5HT) synthesis by L-tryptophan (TRP) injection in malnourished, corn-fed rats.** Federation Proceedings. 35(3):241, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, 5-hydroxytryptophan (5-HTP) levels in tryptophan (TRP) and diluent injected corn and well nourished rats following RO4-4602 (RO) injection were reported. Animals received RO or diluent, followed 10 minutes later by TRP or its diluent, and were killed 30 minutes after the second injection. These results are confirmed by measurements of 5-hydroxytryptamine (5HT) accumulation after pargyline inhibition of monoamine oxidase. The reduction in brain 5HT in corn rats is thus probably due largely to decreased synthesis secondary to substrate deficiency and not an inadequacy of synthetic enzymes. (Journal abstract modified)

238677 Neckers, L. M. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Modulation of brain tryptophan hydroxylase (TPH) activity by brain tryptophan (TP) content.** Federation Priceedings. 35(3):241, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the modulation of brain tryptophan hydroxylase (TRH) activity by brain tryptophan (TP) content was reported. Several conditions which decreased forebrain TP content by 30-50% (neutral amino acid load, chlorimipramine, maintainence on TP deficient diet) increased TPH (30-100%). Dorsal raphe TPH increased (70%) only by the TP deficient diet, which was the only treatment lowering TP in this nucleus (50%). In spinal cord, TP and TPH did not change in any condition studied. In forebrain the increase in TPH caused by several conditions was blocked by TP injection. Increasing TP above control levels had no effect on basal TPH. TP content of various brain regions is not uniformly affected by the conditions tested. A correlation between TPH and TP decrease was found in every central nervous system region. This phenomenon was viewed as a compensatory mechanism stabilizing serotonin (5-HT) synthesis in the face of fluctuations of TP tissue content. (Journal abstract modified)

238678 Meek, James L.; Lofstrandh, Sonja. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Tryptophan hydroxylase in discrete nuclei: comparison of activity in vitro and in vivo.** Federation Proceedings. 25(3):241, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a comparison of activity in tryptophan hydroxylase in vitro and in vivo was reported. The activity of the enzyme in vivo by measuring the accumulation of 5-hydroxytryptophan (5HTP) 45 min after injection of the decarboxylase inhibitor RO4/4602. The 5HTP was measured by high pressure liquid chromatography using fluorescence detection. In the median and dorsal raphe nuclei, 5HTP accumulated at a rate of 30-50 times greater than in caudate nucleus and hippocampus. The rapid synthesis of 5-hydroxytryptamine (5-HT) measured in vivo in the cell bodies suggests that the enzyme has substrate and cofactor available. The 5HT formed in the cell bodies is probably rapidly broken down by monoamine oxidase due to a lack of storage, although some may be functionally active and regulate cell excitability. (Author abstract modified)

238680 Reyes, Edward; Palmer, Gene C. University of New Mexico School of Medicine, Albuquerque, NM 87131 **Cellular localization and kinestic properties of gamma-glutamyl transpeptidase in rat cerebral cortex.** Federation Proceedings. 35(3):242, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, evidence for the localization of gamma-glutamyl transpeptidase (gamma-GTP) within the neuronal, glial and capillary enriched fractions of the rat cerebral cortex was presented. Although the Vmax for the en-

zymes differed among these cellular elements they all exhibited the same Michel's Constant for the substrate. The latter finding implies the same enzyme was assayed in all three cellular fractions. In addition all three factions plus the homogenate exhibited nonlinearity with respect to Lineweaver-Burk double reciprocal plots suggesting the existence of isozymes of gamma-GTP within the brain. Ammonium sulfate fractionation and differential centrifugation suggests that two forms of gamma-GTP are present in brain. The apparent presence of multiple enzyme forms imply that amino acid transport via gamma-GTP is not limited to cappillaries and the operation of the gamma-glutamyl cycle is operative throughout the brain. (Journal abstract modified)

238681 Barkai, Amiram. NYS Psychiatric Institute, New York, NY 10032 **Relationship between serotonin in the intact brain and release of protein into the perfused cerebrospinal fluid compartment of conscious and anesthetized rabbits.** Federation Proceedings. 35(3):242, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the relationship between serotonin (5-HT) turnover (Tr) in the intact brain and release of protein into the perfused cerebrospinal fluid compartment of conscious and anesthesized rabbits was reported. Amine Tr was estimated from the rate of appearance of its metabolite in artificial cerebrospinal fluid (CSF) during ventriculocisternal perfusion. Concentrations of endogenous protein(s) of low molecular weight, which appeared in the perfusate at a relatively constant rate, were also determined. Compared to conscious rabbits, the Tr of 5-HT but not of dopamine decreased (40%) during anesthesia with concomitant reduction (50%) in the rate of appearance of protein(s) in the artificial CSF. Thus, the depression of consciousness by pentobarbital appears to be associated with reduced activity in serotonergic neurons. The correlation between Tr of 5-HT and release of protein(s) into the perfusate indicates that mechanisms underlying the regulation of consciousness may involve secretion of certain protein(s) into the CSF. (Journal abstract modified)

238682 Wright, Jeremy; Cho, Arthur K.; Gal, Joseph. University of California, Los Angeles, CA 90024 **N-hydroxyamphetamine: a major metabolite of amphetamine in rabbit liver extract.** Federation Proceedings. 35(3):243, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the metabolism of d-amphetamine by rabbit liver preparations was presented. Significant amounts of N-hydroxyamphetamine were detected together with the phenyl-2-propanol TFA derivative. Approximately 40% of the amphetamine was metabolized during a 1 hr incubation. Phenylacetone oxime was not detected in incubations up to 1 hr, but appeared in small amounts in 2 hr and 3 hr incubations. Phenylacetone was converted almost quantitatively to phenyl-2-propanol in less than 10 min. Analysis of metabolites and authentic samples revealed that undervitalized N-hydroxyamphetamine, after passage through the column, gave a mass spectrum identical with that of authentic phenylacetone oxime. It was concluded that phenylacetone oxime is at best a minor metabolite of d-amphetamine and that N-hydroxylation is a major pathway in amphetamine metabolism. Results indicate that phenyl-2-propanol is not produced via the N-hydroxy metabolite but by an entirely different route. (Journal abstract modified)

238684 Hucker, H. B.; Balletto, A. J.; Demetriades, J.; Arison, B. H.; Zacchei, A. G. Merck Institute for Therapeutic Research, West Point, PA 19486 **Biotransformation of amitriptyline in the dog.** Federation Proceedings. 35(3):244, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the biotransformation of amitriptyline in the dog was reported. Dogs given 5,10,11-14C-amitriptyline excreted 45% of the dose in the urine in 24 hours. Four of the metabolites identified in dog urine, 10-hydroxyamitriptyline, 10-hydroxynortriptyline, amitriptyline N-oxide and nortriptyline, are also present in the urine of man and other species. Two new metabolites were identified as apparent arene oxide derivatives of amitriptyline and nortriptyline, respectively. These findings represent the first report of arene oxide formation in the tricyclic antidepressant series. (Journal abstract modified)

238686 Musacchio, Jose M.; Craviso, Gale L. Department of Pharmacology, NYU Medical School, New York, NY 10016 **Irreversible inactivation of the opiate receptor by the alkylating local anesthetic W12099.** Federation Proceedings. 35(3):263, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the irreversible inactivation of the opiate receptor by the alkylating local anesthetic W12099 was reported. The opiate receptor in mouse brain homogenates is irreversibly inactivated by incubation with an alkylating chloroethyl analog of lidocaine, W12099 (2-((2-chloroethyl)ethylamino)-2',6'-acetoxylidide HCl). The inactivation process follows pseudo first order kinetics and is strongly temperature dependent. The fraction of opiate receptors which is not inactivated in a given period of time retains its original affinity for naltrexone. The alkylation produced by W12099 cannot be reversed by washing or by 1 milliM mercaptoethanol or Cleland's reagent. In either the presence or absence of sodium, opiate agonists and antagonists are equally effective at their respective mean effective dose (ED50) concentrations in protecting the receptor from inactivation; dextrophan, an inactive isomer, does not protect from inactivation. Dibenzamine and phenoxybenzamine, alkylating alpha-adrenergic blocking agents which contain chloroethylamine groups as in W12099, also irreversibly inactivate the opiate receptor. (Journal abstract modified)

238688 Tessel, Richard E.; Rutledge, Charles O. Department of Pharmacology, School of Pharmacy, University of Kansas, Lawrence, KS 66045 **The effect of pargyline on the release of endogenous norepinephrine by N-ethylamphetamine and fenfluramine.** Federation Proceedings. 35(3):266, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effect of pargyline on the release of endogenous norepinephrine (NE) by N-ethylamphetamine (NEA) and fenfluramine (FENF) was reported. Total tissue NE was markedly increased after in vivo pargyline and the amount of NE released by each drug was potentiated. Pargyline administration had little effect on the percentage of total NE released by either drug. Pargyline in vitro had little effect on NEA induced release of NE and potentiated FENF induced NE release. The data suggest that the potentiation of the effects of NEA and FENF after in vivo pargyline may involve increased amounts of NE released from an enlarged neuronal store of NE. (Journal abstract modified)

238689 Ziance, R. J. Department of Pharmacology, University of Georgia School of Pharmacy, Athens, GA 30602 **Effect of monoamine oxidase inhibitors on release and uptake of 3H-norepinephrine in rat cerebral cortex in vitro.** Federation Proceedings. 35(3):266, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effect of monoamine

oxidase inhibitors on release and uptake of 3H-norepinephrine (3H-NE) in rat cerebral cortex was reported in vitro. Incubation of chopped rat cerebral cortex tissue with 3H-norepinephrine (NE) was followed by iproniazid (ipron), tranylcypromine (tranyl), d-amphetamine (amph), phenelzine (phen), pheniprazine (phenip) or pargyline (parg). Amph and tranyl were the most potent whereas ipron and phen were the least potent of the releasing agents. Inhibition of 3H-NE uptake did not make a significant contribution to drug induced release of 3H-NE since parg did not inhibit 3H-NE but was able to increase the release of 3H-NE from rat cerebral cortex tissue. (Journal abstract modified)

238690 Langley, A.; Weiner, N. Department of Pharmacology, University of Colorado Medical School, Denver, CO 80220 **Release of norepinephrine (NE) and dopamine-beta-hydroxylase (DBH): effect of phenoxybenzamine (PBZ) alone and in combination with 8-bromo-cGMP and dibutyryl cAMP.** Federation Proceedings. 35(3):266, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effect of phenoxybenzamine (PBZ) on the release of norepinephrine (NE) and dopamine-beta-hydroxylase (DBH) in sympathetic nerves to the pig heart was reported. PBZ was perfused through the heart beginning immediately after stimulation 2 (S-2) and continuing through stimulation 6 (S-6). In some experiments, cyclic nucleotide analogs were perfused through the heart beginning 15 min prior to S-2, and continuing throughout the remainder of the experiment. The outflow of total 3H, 3H-NE, endogenous NE, and DBH activity was measured for all stimulations. PBZ produced an increase above control in release of total 3H and 3H-NE with S-3. At S-6 both total 3H and 3H-NE outflow were still more than twice control values. PBZ also increased NE outflow above control levels and increased output of DBH activity to twice that of control. 8-Bromo-cyclic-guanosine monophosphate elevated the augmenting effecting effect of PBZ on all the measured indices of release. The increase in DBH release in the presence of both substances was more modest. Dibutyryl-cyclic adenosine monophosphate produced similar effects at lower concentrations of this cyclic nucleotide. (Journal abstract modified)

238691 Fuller, Ray W.; Ho, Peter P. K.; Snoddy, Harold D. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Inhibition of dopamine beta-hydroxylase by some analogs of methimazole.** Federation Proceedings. 35(3):267, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of several analogs of methimazole on adrenal dopamine-beta-hydroxylase (DBH) in vitro and on norepinephrine levels in rat brain and heart were reported. Replacement of the methyl group in methimazole with ethyl, n-propyl, isobutyl, isopentyl, 2-heptyl, or cyclohexyl groups increased the activity of 2-mercaptoimidazoles as DBH inhibitors in vitro and in vivo. When 1-cyclohexyl-2-mercaptoimidazole was injected into rats, brain norepinephrine levels declined exponentially for 90 min at a rate that was decreased by clonidine or desipramine pretreatment. Brain norepinephrine was depleted maximally at 2-4 hrs and had returned to control levels within 16-24 hrs. Repletion of heart norepinephrine by dopamine in metaraminol pretreated rats was prevented. Adrenal catecholamine levels were decreased in exercised rats (with accelerated turnover of catecholamines) but not in control rats. Brain and heart norepinephrine levels were depressed more in exercised rats than in controls. (Journal abstract modified)

238692 Richelson, E. Department of Psychiatry, Mayo Foundation, Rochester, MN 55901 **Properties of tyrosine hydroxylation in living mouse neuroblastoma cells.** Federation Proceedings. 35(3):267, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of tyrosine hydroxylation in intact cells of mouse neuroblastoma clone NIE-115 which have high levels of tyrosine-3-hydroxylase (TH) was presented. A cholinergic clone (NS-20) and a rat glioma clone (C6) did not produce significant amounts of (3H)OH. Tyrosine hydroxylation was dependent on time of incubation, cell number, and the concentration of L93,5-3H)tyrosine in the medium. Substrate inhibition occurred with tyrosine concentrations between 20 and 50 microM. The reaction was twice as fast at pH 5.5as at pH 7.4. L-3-iodotyrosine was a competitive inhibitor. Dopamine was a noncompetitive inhibitor. 1-Norepinephrine had no effect. High or low concentrations of monovalent and divalent cations and cyclic nucleotides had no major effect on the reaction. These results show that the hydroxylation of tyrosine by living N1E-115 cells has many of the properties of the reaction catalyzed by purified TH from normal tissue. (Journal abstract modified)

238693 Ingall, G. B.; Kogan, F. J.; Gibb, J. W. Department of Pharmacology, University of Utah, Salt Lake City, UT 84112 **Effect of methamphetamine and neuroleptic agents on the kinetic properties of striatal tyrosine hydroxylase.** Federation Proceedings. 35(3):267, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effect of methamphetamine (Meth) and neuroleptic agents on the kinetic properties of striatal tyrosine hydroxylase (TH) was reported. Following treatment with Meth, the apparent maximum velocity of striatal TH declined by 56%. The apparent Michaelis constant of the enzyme for the cofactor was unaffected. Further studies demonstrated that the increase in striatal TH activity following the acute administration of haloperidol or reserpine is sensitive to the ionic concentration of the assay medium. The increase in TH activity caused by haloperidol or reserpine was reduced to 10% of control by increasing the buffer concentration from 0.1to 0.7M. The Meth-induced decline in TH activity was unaffected by changes in ionic concentration. (Journal abstract modified)

238695 Horita, A.; Carino, M. A. University of Washington, Seattle, WA 98195 **Effect of PCPA and methergoline on the pentobarbital-TRH interaction in rabbits.** Federation Proceedings. 35(3):268, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effect of parachlorophenylalanine (PCPA) and methergoline on the pentobarbital (PB)/thyrotropin-releasing-hormone (TRH) interaction in rabbits was reported. While control animals slept for 82 min after PB, those pretreated with PCPA slept for 168 min, indicating that lowered brain levels of 5-hydroxytryptophan (5-HT) potentiate PB anesthesia. Control PB animals awoke within 10-15 min after TRH, but PCPA pretreated animals did not recover until 94 min after TRH. The analeptic effect of TRH was therefore markedly attenuated in the PCPA pretreated animal. After restoration of brain 5-HT levels with carbidopa plus 5-hydroxytryptophan (5-HTP) PB exerted its normal duration of narcosis, and the analeptic effectiveness of TRH was partially restored. In other experiments, methergoline was employed as an anti-5-HT compound. It greatly potentiated the duration of PB narcosis, but was ineffective in attenuating the analeptic effect of TRH. It is concluded that

brain 5-HT may influence PB effects and its antagonism by TRH. (Journal abstract modified)

238699 Gale, Karen N. University of Washington, Seattle, WA 98195 **Dopamine agonist-induced asymmetry after lesions of superior colliculus in rats.** Federation Proceedings. 35(3):269, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, dopamine agonist induced asymmetry after lesions of superior colliculus (SC) in rats was reported. The dopaminergic (DA) agonists apomorphine and d-amphetamine enhanced motor asymmetry. Within a week postoperatively the spontaneous asymmetry disappeared, but pronounced circling was still induced by drug treatment. Control lesions restricted to cortex, dorsal to SC, did not result in drug induced asymmetry. Pharmacological responses of SC lesioned rats resembled those obtained after lesions in caudate putamen or substantia nigra. Unilateral SC lesions were able to counteract the effect of contralaterally placed caudate lesions. The results suggest that DA agonist induced rotation may not depend solely or specifically upon bilateral imbalance in the nigrostriatal system, but instead may reflect more generalized asymmetrical functioning in sensorimotor integration. The data indicate an interrelationship between caudate and SC. Effects of SC lesions on DA function in caudate are currently being investigated. (Journal abstract modified)

238700 Baylor, M. R.; Stitzel, R. E.; Azzaro, A. J. Department of Pharmacology, West Virginia University Medical Center, Morgantown, WV 26506 **Effects of dopamine (DA) derivatives on central dopaminergic mechanisms.** Federation Proceedings. 35(3):269, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the effects of primary, secondary, and tertiary amine derivatives of dopamine (DA) on central DA activity was reported. The primary and secondary amines appeared to be more effective in inhibiting the DA neuronal transport system when compared to the tertiary amines. It would appear from these results that while acetylation of the phenolic hydroxyls may enhance lipophilicity, the primary requirement for central dopaminergic activity in vivo is demethylation of the nitrogen atom. Since this same molecular arrangement produces a relatively weak inhibition of the striatal DA uptake systems, the central DA activity of the tertiary amine derivatives appears to result from the direct stimulation of postsynaptic DA receptors. Studies on rotational behavior after 6-OHDA and the in vitro release of DA may further clarify the nature of the central DA activity. (Journal abstract modified)

238701 Siew, C.; Goldstein, D. B. Department of Pharmacology, Standford University School of Medicine, Stanford, CA 94305 **A novel method for rapid development of barbiturate tolerance and physical dependence in mice.** Federation Proceedings. 35(3):269, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a method for rapid development of barbiturate tolerance and physical dependence in mice was reported. Functional tolerance was shown by a significant decrease in sleep time after a challenge dose of barbital administered 24 hr after withdrawal (i.e.,after drug delivery ceased). Physical dependence was shown by central nervous system hyperexcitability after withdrawal, as measured either with pentylenetetrazol (PTZ) or by convulsions elicited by handling. At 16 hr after withdrawal, 85% of the mice showed tonic extensor seizures at a dose of PTZ that caused seizures in only 30% of naive mice. PTZ injections at different intervals after withdrawal showed a progressive rise in a seizure susceptibility up to 16 hr.,followed by a return to control values by 56 hr. Convulsions on handling were seen on withdrawal after 8 days of sodium barbital administration. It was concluded that the osmotic pumps may be useful in studies of the mechanisms of barbiturate tolerance and dependence. (Journal abstract modified)

238702 Chou, D. D. T.; Wang, S. C. Department of Pharmacology, College of Physicians & Surgeons, Columbia University, New York, NY 10032 **Effects of morphine and benzodiazepines on limbic system.** Federation Proceedings. 35(3):269, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of morphine and two benzodiazepine derivatives, diazepam and chlordiazepoxide, on single unit activity of amygdaloid nuclear complex and hippocampal formation were reported in cats. Diazepam or chlordiazepoxide depressed both spontaneous and sciatic nerve evoked activity of neurons in these two areas. The spontaneous and nerve evoked firing rates of both amygdaloid and hippocampal neurons were augmented by morphine sulfate. The morphine induced augmentation of hippocampal, but not amygdaloid, neuronal activity was effectively antagonized by naloxone. Diazepam and chlordiazepoxide were capable of preventing or converting the action of morphine on neuronal activity on these two areas and the effects were dose dependent. Results suggest that in the cat amygdala and hippocampal formation may be an important site of morphine action to induce the behavioral responses and that these two neuronal structures are the possible sites of tranquilizing actions of diazepam and chlordiazepoxide. (Journal abstract modified)

238703 Pickworth, W. B.; Sharpe, L. G. NIDA Addiction Research Center, Lexington, KY 40511 **The transcallosally evoked potential (TEP) following administration of LSD, mescaline, DMT, apomorphine and methoxamine in the dog.** Federation Proceedings. 35(3):270, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the changes in the transcallosally evoked potential (TEP) following lysergic acid diethylamide (LSD), apomorphine, and methoxine was reported in the dog. LSD significantly depressed the TEP and the effect persisted for at least 80 minutes. DMT caused a significant and reversible increase in the amplitude of the TEP. LSD and dimethyl tyrosine (DMT) reduced the alpha activity of the electroencephalogram and enhanced the amplitude of delta and theta waves. DMT produced a significant and LSD a marginal increase in electrogenesis. Tryptamine, mescaline, methoxamine, and apomorphine had no significant effect on the TEP or Electroencephalogram. These results suggest that depression of the TEP is not correlated with either reflex facilitation in the dog or hallucinogenic activity in man. (Journal abstract modified)

238708 Shih, T.-M.; Khachaturian, Z. S.; Reisler, K. L.; Rizk, M. M.; Hanin, I. Department of Psychiatry, WPIC, School of Medicine, University of Pittsburgh, Pittsburgh, PA 15261 **Methylphenidate as a cholinergic agonist: further observations.** Federation Proceedings. 35(3):307, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the effect of methylphenidate (MPH) on acetylcholine (ACh) turnover rate in rat brain in vivo was reported. The results indicate that

MPH increases significantly the ACh turnover rate in the midbrain, but has only a mild effect on cortex. These findings complement observations that MPH and cholinergic agonists (oxotremorine and nicotine) attenuate unit activity (UA) in rat midbrain reticular formation (MRF), presumably via an inhibitory cholinergic link. The effect of MPH on UA in the MRF of two groups of rats was investigated. In control rats MPH attenuated UA by 37% with a latency of 10 min. In another group of rats, rendered hyperactive by lead ingestion since birth, the attenuation of UA induced by MPH was reduced (20%) and the latency of its effect delayed (50 min). The findings (neurochemical and electrophysiological) provide further evidence for a central cholinergic role of MPH. (Journal abstract modified)

238709 Donelson, Alan C.; Domino, Edward F. Department of Pharmacology, University of Michigan, Ann Arbor, MI 48104 **Effects of (-)delta9-tetrahydrocannabinol on regional brain acetylcholine in the rat.** Federation Proceedings. 35(3):307, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the regional utilization of brain acetylcholine (ACH) after injection of (-)delta9-tetrahydrocannabinol (THC) was presented. ACH levels in the hypothalamus, thalamus, hippocampus, and caudate nucelus were assayed. Regional levels of ACH in the rat brain were not significantly altered by 10mg/kg THC i.p. to control animals. Furthermore, no significant alterations of ACH utilization were found in the hypothalamus, thalamus, and caudate nucleus. However, the previously depleted hippocampal levels of ACH increased in a dose/effect manner. The increases ranged from 123% to 243%. The results suggest that THC acts in the hippocampus to reduce ACH utilization. (Journal abstract modified)

238710 Frank, G. B.; Buttar, H. S.; Marwaha, J.; Durham, H. D. University of Alberta, Edmonton, Alberta, Canada **Lack of a relation between the anti-psychotic and the excitability depressant properties of major tranquilizers.** Federation Proceedings. 35(3):308, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of haloperidol, chlorpromazine, and promethazine on action potential (AP) production in frog sartorius muscle fibers were reported. All three drugs suppressed excitability without altering resting membrane potential or the input resistance measured with intracellular microelectrodes, but the threshold current and threshold depolarization were significantly increased. Depressant effects on AP rate of rise were competitively antagonized by increasing the sodium concentration of the bathing solution, indicating that the drugs act by inhibiting the specific increase in sodium conductivity. The inhibitory effect of haloperidol, but not of chlorpromazine, was partially antagonized by the addition of naloxone, indicating an effect of haloperidol on opiate receptors. It is concluded that the antipsychotic effects of chlorpromazine and promethazine are not related to their anesthetic like effects or to an effect on the opiate receptor associated with the sodium channel. (Journal abstract)

238712 Parmar, S. S.; Jaiswal, R. K.; Kumar, S.; Barthwal, J. P.; De Boer, B. Department of Physiology, University of North Dakota, School of Medicine, Grand Forks, ND 58202 **Anticonvulsant activity of newer substituted triazoles.** Federation Proceedings. 35(3):308, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the anticonvulsant activity of newer substituted triazoles was reported. Nine 5-(3,4,5-trimethoxyphenyl)-4-substituted phenyl-3-hydrazinocarbonylmethylthio-1,2,4(H)triazoles (TMHT) were synthesized and evaluated for their anticonvulsant, monoamine oxidase (MAO) inhibitory and antiproteolytic properties. TMHT provided 20-90% protection against pentylene tetrazol induced convulsions in mice where introduction of the substituent in the phenyl nucleus at position 4 resulted in increased activity. 2-Methoxyphenyl substituted triazole showed maximum anticonvulsant activity. Introduction of the substituent in the phenyl nucleus at position 4 caused decrease in MAO inhibition. TMHT provided 22-77% protection against trypsin induced hydrolysis of bovine serum albumin. The results indicate that MAO inhibitory and antiproteolytic properties cannot provide the biochemical basis for the anticonvulsant activity of TMHT. (Journal abstract modified)

238714 Weiss, George B. Department of Pharmacology, University of Texas Southwestern Medical School, Dallas, TX 75235 **Alterations in 45Ca uptake and efflux in rat cortex, striatum and hypothalamus slices.** Federation Proceedings. 35(3):325, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the uptake and efflux of 45 calcium (45Ca) in rat brain area slices was reported. Findings indicate that Ca++ distribution is similar in slices from different rat brain areas, 45Ca binding is increased in Ca++ depleted tissues, loss of 45Ca is an energy dependent process which is at least partially coupled to Ca++ uptake, decreased temperature inhibits Ca++ extrusion, lanthanum ion impedes uptake and subsequent binding of Ca++, and strontium ion does not prevent 45Ca uptake at cellular binding sites. Pharmacological agents may also alter the bound cellular Ca++ fraction and, in this manner, may affect responsiveness of the neuronal membrane and modulate endogenous neurotransmitter release. (Journal abstract modified)

238715 Hruska, R. E.; Huxtable, R. J.; Bressler, R.; Yamamura, H. I. Department of Pharmacology, College of Medicine, University of Arizona, Tucson, AZ 85724 **Taurine: a sodium-dependent high affinity uptake system into synaptosomes of rat brain.** Federation Proceedings. 35(3):325, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the uptake of 3H-taurine into synaptosomal enriched fractions of whole rat brain was presented. The data were best satisfied by the assumption of two transport components: a high affinity uptake system and a low affinity system. The high affinity transport system exhibited an absolute dependency upon sodium ions, and was markedly inhibited by ouabain and metabolic uncouplers. Regional distribution of taurine transport resulted in the highest accumulation in the midbrain and cerebral cortex, and with lowest accumulation in the cerebellum and spinal cord. Hypotaurine, beta-alanine and gamma-aminobutyric acid (GABA) at 100 microM concentrations inhibited the high affinity taurine uptake 96, 72, and 54%, respectively. These findings are consistent with taurine functioning as a neurotransmitter in the brain. (Journal abstract modified)

238716 Shellenberger, M. K.; Young, D. N.; Levine, M. S. Department of Pharmacology, Mental Retardation Research Center, KUMC, Kansas City, KS 66103 **Effects of intracerebroventricular L-dopa on caudate unit firing.** Federation Proceedings. 35(3):325, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of in-

tracerebroventricular L-dopa on caudate unit firing were reported. Extracellular recordings of single units were made from both caudates using micropipettes. Injection of L-dopa into one ventricle produced bilateral caudate unit silence, lasting 30-40 min, coincident with a reduction in systolic blood pressure and cardiac slowing. Upon recovery, units recorded in the contralateral caudate had mean interspike intervals significantly longer than in Merlis controls or the ipsilateral side. By 3 hrs this contralateral slowing was gone. It is suggested that the unit silence and cardiovascular response were from actions of L-dopa on lower brainstem structures. The data indicate that L-dopa was acting on the ipsilateral caudate or other basal ganglia structures as well, although the time course of the effect would seem to rule out a direct action of the unaltered L-dopa molecule. (Journal abstract modified)

238719 Liebschutz, J.; Moskowitz, M. A.; Munro, H. N.; Nowak, T.; Rubin, D. C.; Wurtman, R. J.; Wolf, G. MIT, Cambridge, MA 02139 **Necessity of hyperthermia for L-dopa or d-amphetamine to disaggregate rat brain polysomes.** Federation Proceedings. 35(3):326, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, evidence that hyperthermia must occur to allow disaggregation of rat brain polysomes was presented. It is not known whether hyperthermia per se causes brain polysome disaggregation, or whether hyperthermia must accompany the other pharmacological actions of dopa and amphetamine. In vitro suppression of protein synthesis by amphetamine suggests the latter mechanism. (Journal abstract modified)

238723 Peters, Marvin A.; Thaete, Larry G. Department of Pharmacology, Loma Linda University School of Medicine, Loma Linda, CA 92354 **Development of brain cerebrosides and cerebroside sulfate (sulfatide) in offspring of control rats and rats chronically treated with methadone.** Federation Proceedings. 35(3):385, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the development of brain cerebrosides and cerebroside sulfate on offspring of rats treated chronically with methadone was reported. Results show no significant differences between control and chronically treated animals; however, differences were found in the pattern of development of total cerebrosides and sulfatides. Some regional differences in the pattern of sulfatide development were observed. The development of total cerebrosides is most rapid between days 15 and 25 and reaches a stable level in all brain regions studied, whereas the sulfatides develop most rapidly between days 10 and 14 in all areas studied with subsequent leveling off in the brainstem and midbrain areas, but a marked drop off in content was seen in the cerebellum and cerebral tissues. (Journal abstract modified)

238724 Van Buren, Janice. Astra Pharmaceutical Products, Inc., Worcester, MA 01606 **Differentiation of sensory-motor mechanisms in peripheral nerve block by modified rat-sciatic block method.** Federation Proceedings. 35(3):403, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, modifications of the in vivo rat sciatic block model made to separate effects of local anesthetics on sensory and motor mechanisms were reported. The effects of various treatments on grasping reflex and on vocal pain response to noxious electrical stimulation of the hindfoot were monitored. Control studies indicate that the procedure itself does not alter pain threshold, nor are rats conditioned within experimental time. Rises in pain threshold were induced by sciatic lidocaine and systemic morphine sulfate. Changes in stimulation frequency provided further differentiation between effects of morphine and local anesthetics, as well as between doses of bypivacaine, etidocaine, lidocaine and tetracaine. The modified model successfully detected gradations in sensory block in addition to differences in sensory and motor durations and serves as a useful screen for local anesthetic agents. (Journal abstract modified)

238725 Diamond, B. I.; Sabelli, H. C.; Havdala, H. S. Mt. Sinai Hospital, Chicago, IL 60608 **Differential interactions of pentobarbital and phenobarbital with beta-adrenergic mechanisms.** Federation Proceedings. 35(3):404, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, differential interactions of pentobarbital (PENTO) and phenobarbital (PHENO) with beta-adrenergic mechanisms were reported. The spike amplitude lowering effect of PENTO is enhanced by concomitant administration of L-epinephrine, and reduced by the beta-blockers sotalol and L-propranolol, but not by the local anesthetic D-propranolol or by the alpha-blocker phentolamine. In contrast, the spike amplitude lowering effect of PHENO was not altered by L-epinephrine, L-propranolol or phentolamine. Interactions with the epinephrine second messengers cyclic adenosine monophosphate and calcium also differentiated PHENO from PENTO. In the maximal electroshock test (mouse), sotalol and L-propranolol enhanced the anticonvulsant effect of PENTO without altering that of PHENO. PENTO and PHENO also differed in their interactions with gamma-aminobutyric and other putative neurotransmitters in peripheral nerves. The experiments suggest that PHENO and PENTO differentially affect membrane receptors, particularly beta-adrenergic mechanisms. (Journal abstract modified)

238726 Chiel, Hillel J.; Wurtman, Richard J. MIT, Cambridge, MA 02139 **Antagonisms by neutral amino acids (NAA) of the hypothermic effect of d-amphetamine (AMP).** Federation Proceedings. 35(3):405, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the antagonism by neutral amino acids (NAA) of the hypothermic effect of d-amphetamine (AMP) was reported. Rats received valine (VAL) or other amino acids or saline (SAL), and, 30 min later, AMP or SAL; they were then placed in the cold. Body temperatures were measured after each injection and every 30 min thereafter. After 60 min in the cold, when the hypothermic effect was maximal, VAL significantly blocked the AMP effect but caused no significant hypothermia alone. Alanine, glutamic acid and arginine failed to block the hypothermia, while leucine and isoleucine succeeded; lysine, which lowers brain tyrosine, also suppressed it. These data affirm that tyrosine administration of amino acids which do not affect catecholamine (CA) producing enzymes can modify brain CA synthesis by changing brain tyrosine, and such acute changes in CA synthesis modify synaptic function. (Journal abstract modified)

238727 Terrell, Christine L.; Beck, Lloyd. Department of Pharmacology, University of Minnesota, Duluth, MN 55812 **Evidence for a beta-adrenergic receptor mediated positive feedback mechanism regulating release of norepinephrine.** Federation Proceedings. 35(3):405, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, evidence for a beta-adrenergic receptor mediated positive feedback mechanism regulat-

ing release of norepinephrine was presented. Observations with phenoxybenzamine conducted in the autoperfused hindlimb of the dog indicate a greater blockade of neurally induced vasoconstriction than of vasoconstriction induced by intraarterial injection of norepinephrine, an observation in accord with a positive alpha-adrenergic, rather than a negative alpha-adrenergic feedback mechanism. Results show that beta-adrenergic blocking agents significantly potentiate the response to intraarterially injected norepinephrine without potentiating nerve induced vasoconstriction over the frequency range of 0.1-12.8Hz, suggesting the existence of a positive beta-adrenergic feedback mechanism as well. (Journal abstract modified)

238728 Everett, Guy M. Department of Pharmacology, Univeristy of California, San Francisco, CA 94143 **Comparative pharmacology of amphetamine and pemoline on biogenic amine systems.** Federation Proceedings. 35(3):405, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the comparative pharmacology of amphetamine and pemoline on biogenic amine systems was reported. Amphetamine has major effects on central dopamine (DA) systems, increasing release and turnover. It also has similar effects on both peripheral and central norepinephrine (NE) systems. In addition, amphetamine has direct action on DA and NE receptors. Such multiple effects of amphetamine make it difficult to determine the specific role of DA and NE behavioral states and has led to much confusion. Pemoline, a long-acting central stimulant, has more specific effects. It does not release NE peripherally (no cardiovascular effects) nor increase NE turnover in brain. Pemoline increases DA turnover in caudate and produces stereotyped activity. In contrast to amphetamine, pemoline does not reverse resperpine depression in mice unless pretreatment with dopa is given. Pemoline apparently has no direct action on postsynaptic receptors and acts by releasing dopamine onto receptor sites. (Journal abstract)

238729 Patrick, Robert L.; Barchas, Jack D. Department of Psychiatry, Stanford University, School of Medicine, Stanford, CA 94305 **Endogenous dopamine release-dependent and independent activation of dopamine synthesis in rat brain striatal synaptosomes.** Federation Proceedings. 35(3):406, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, endogenous dopamine release dependent and independent activation of dopamine synthesis in rat brain was reported. Dopamine synthesis in rat brain striatal synaptosomes was activated by depolarizing concentrations of veratridine (75 microM), by 1mM dibutyryl cAMP adenosine monophosphate (AMP) (N6,O2-dibutyryl adenosine-3',5'cyclic monophosphoric acid) and by the tyrosine hydroxylase cofactor 6-MPH4 (DL-6-methyl 5,6,7,8-tetrahydropterine) at 0.1mM. Veratridine produced a calcium dependent increase in endogenous dopamine release, while dibutyryl cAMP and 6-MPH4 did not stimulate release. Tyramine produced a calcium independent increase in dopamine release and an inhibition of synthesis. These data suggest that dopamine synthesis can be stimulated independently of endogenous dopamine release, and that dopamine releasing agents may have differential effects upon dopamine synthesis, depending on their mechanism of release. (Journal abstract)

238730 Shore, P. A. University of Texas Health Science Center, Dallas, TX 75235 **Amfonelic acid facilitation of impulse-induced striatal dopamine release.** Federation Proceedings. 35(3):406, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, amfonelic acid (AFA) facilitation of impulse-induced striatal dopamine (DA) release was reported. Results indicate that AFA does not lower striatal DA and only slightly elevates striatal homovanillic acid (HVA) and dihydroxyphenylacetic acid (DOPAC). However, low doses of AFA greatly enhance the striatal HVA and DOPAC elevation seen after haloperidol. After blockade of tyrosine hydroxylase AFA alone has little effect on DA levels but markedly potentiates the DA lowering seen with haloperidol. This effect is blocked by the DA receptor agonist, apomorphine, or by gamma-butyrolactone, an inhibitor of nigrostriatal impulse flow. Methylphenidate shares AFA's action on DA release but is weaker. Other agents including cocaine, d-amphetamine or l-amphetamine, morphine, desipramine, and benztropine mesylate are inactive, even though some of these drugs are reported to inhibit striatal DA reuptake, AFA did not act similarly on hypothalamic norepinephrine. (Journal abstract modified)

238731 Dorris, R. L. Department of Pharmacology, Baylor College of Dentistry, Dallas, TX 75226 **Release of 3H-alpha-methyl-meta-tyramine from corpus striatum in vitro and the effects of glucose deprivation.** Federation Proceedings. 35(3):406, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the facilitation of impulse-induced striatal dopamine release by amfonelic acid was reported. Release of the tritiated false dopaminergic transmitter, alpha-methyl-m-tyramine (MMTA) from rat striatum was studied in vitro. After its initial uptake by pieces of striatal tissue, 3H-MMTA was released by high potassium (K+) and by amphetamine. The release by high K+ was calcium dependent and prior reserpinization of animals made tissue 3H-MMTA highly resistant to release by K+, but not by amphetamine. The omission of glucose greatly augmented the releasing effects of K+ and amphetamine. The effect of glucose could not be ascribed to an action on reuptake as no significant decrease in uptake could be demonstrated by the omission of glucose from the incubation medium. A concentration of cocaine which markedly inhibited uptake failed to mimic the effect of zero glucose in augmenting release. (Journal abstract modified)

238732 Rivera-Calimlim, Leonor. University of Rochester, Rochester, NY 14642 **Interaction of trihexyphenidyl and chlorpromazine: probable mechanism.** Federation Proceedings. 35(3):408, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the interaction of trihexyphenidyl (THP, Artane) and chlorpromazine (CPZ) in adult male rats was reported. The absorption and tissue distribution of oral 14C-CPZ were compared in THP treated and non-treated rats. The total radioactivity (CPZ) in the plasma and brain of rats treated with THP was significantly lower, whereas total radioactivity in the gut was significantly higher than in rats not previously treated with THP. THP treatment was not shown to affect transport of 14C-CPZ in everted sacs, nor to affect the metabolism of 14C-CPZ by liver homogenates, but THP significantly delayed gastric emptying, as measured by gastric clearance of a marker, 14C-polyethylene glycol. The low plasma and brain levels of oral 14C-CPZ in THP treated rats appeared to be due to decreased absorption because of delayed gastric emptying, and this may also be the mechanism involved in the failure of some psychiatric patients to achieve adequate plasma levels of CPZ when it is combined with THP. (Journal abstract modified)

238734 Geiger, P. F.; Ramos, J. S.; Jobe, P. C. N.E. Louisiana University, Monroe, LA 71201 **Modification of pentylenetetrazol-induced convulsions by drugs which alter brain catecholamine levels or stimulate catecholamine receptors.** Federation Proceedings. 35(3):427, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study to determine whether treatments which alter the catecholamine content of the brain also affect chemoshock seizure (CS) intensity in a manner similar to electroshock (ES) was reported. A small dose of pentylentrazol (PTZ) routinely produced chronic seizure, whereas a larger dose produced tonic seizure. CS produced by PTZ (small dose) were enhanced by Ro4-1284. Systemic administration of L-dopa alone or L-dopa plus Ro4-4602, a peripheral decarboxylase inhibitor, did not antagonize the CS enhancing effects of Ro4-1284. However, L-dopa plus iproniazid antagonized CS induced by PTZ (large dose). Intracerebroventricularly administered (ICVA) norepinephrine (NE) or dopamine (DA) antagonized CS enhancing effects of Ro4-1284, whereas ICVA NE or DA in the absence of Ro4-1284 did not affect CS induced by PTZ (large dose). Apomorphine, a DA receptor stimulant, intensified CS. The data support the concept that NE but not DA acts as an endogenous attenuator of chemoshock seizure intensity in rats. (Journal abstract modified)

238735 Dittrich, Vincent T.; Cole, Henry F.; Tuttle, Warren W. University of Missouri, Kansas City, MO 64110 **Alterations of the EEG of extrapyramidal nuclei following 6-hydroxydopamine lesions.** Federation Proceedings. 35(3):427, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the functional interrelations among extrapyramidal nuclei was reported. Electrode cannulae were placed in the head of the caudate nucleus (CN) of cats; integrated electroencephalograms (EEGs) were recorded from the CN, substantia nigra (SN), globus pallidus (GP), and putamen. Results indicate that the mean integrated activity (MIA) of the CN cortex was depressed more by dopamine than by gamma-aminobutyric acid (GABA). MIA was elevated by physostigmine. In the CN medulla, activity was depressed by physostigmine, dopamine, and GABA, in descending order of effectiveness. Lesion of the SN with 6-hydroxydopamine (6OHDA) decreased MIA from all areas except the putamen, where activity more than doubled. Following 6OHDA, CN cortex MIA was depressed by dopamine, physostigmine, and GABA. (Journal abstract modified)

238736 Donlon, Mildred; McCarthy, Kenneth; Livengood, David; Shain, William. AFRRI, National Naval Medical Center, Bethesda, MD 20014 **Evidence for a dopamine receptor antibody.** Federation Proceedings. 35(3):427, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, evidence for a dopamine (DA) receptor antibody was presented. Antiserum to the somatic cell hybrid TCX11 was produced to obtain an antibody to the DA receptor found on these cells. TCX11 is a subclone of NX31 (a neuroblastoma X embryonic mouse sympathetic ganglion cell hybrid). Intracellular recordings from TCX11 show a depolarizing, conductance increase response upon iontophoretic application of DA. The response is specific in that DA antagonists block the response, agonists mimic DA, and cholinergic antagonists are without effect. Cells were grown in dibutyryl cyclic AMP to induce differentiation, harvested, washed, concentrated, and injected into rabbit footpads. After a period of repeated smaller injections, serum was collected and decomplemented. Bath applications of antiserum showed a dose dependent inhibition of the DA response while control serum was without effect. (Journal abstract modified)

238737 Myslinski, N. R.; Thut, P. D.; Burgison, R. M. University of Maryland, School of Dentistry, Baltimore, MD 21201 **The role of dopamine (DA) and serotonin (5-HT) in the prolongation of post-decapitation convulsions (PDC) in mice.** Federation Proceedings. 35(3):427, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the role of dopamine (DA) and serotonin (5-HT) in the prolongation of postdecapitation convulsions (PDC) in mice was reported. L-dopa after RO4-4602 pretreatment, increased the duration of PDC in mice by approximately 40%. Assays of brains at the time of decapitation showed a 300% increase in DA, an 80% reduction in 5-HT and no change in norepinephrine (NE) levels. The effect of L-dopa on PDC was not blocked by haloperidol, a blocker of DA receptors, nor was it blocked by diethyldithiocarbamate, an inhibitior of (NE) synthesis. p-Chlorphenylalanine produced a 80% reduction in 5-HT and produced a prolongation of PDC similar to that observed after L-dopa. Neither the 5-HT precursor, 5-hydroxytryptophan, nor the 5-HT antagonists, cyproheptadine, methysergid or cinanserin, produced any change in PDC. The results suggest that L-dopa acts by depleting 5-HT in bulbospinal pathways thus enhancing reflex activity in the spinal cord. (Journal abstract)

238739 Wilkening, Doug; Mishra, Ram K.; Makman, Maynard H. Albert Einstein College of Medicine, 1300 Morris Park Ave, Bronx, NY 10461 **Effects of morphine on dopamine-stimulated adenylate cyclase and on cyclic GMP formation in monkey brain amygdala.** Federation Proceedings. 35(3):428, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of morphine (MOR) on dopamine (DA) stimulated adenylate cyclase (AC) and on cyclic guanosine monophosphate (GMP) formation in monky brain amygdala were reported. Adenylate cyclase (AC) activity in homogenates of amygdala was increased approximately 1-fold in the presence of either DA or sodium fluoride (NaF). MOR did not significantly affect the basal AC activity, but in the presence of MOR the stimulation by DA or NaF was reduced. The data suggest an action of MOR at a receptor site distinct from the DA receptor, but functionally related to it. In addition, the cyclic GMP content of amygdala slices was reduced by 70-80% during incubation for 5-20 minutes with MOR. MOR was without effect on cyclic GMP levels in slices of cerebellum, a brain region low in MOR binding receptors. The data indicate that MOR receptors in monkey brain amygdala are functionally concerned with both guanylate cyclase and DA sensitive adenylate cyclase systems. (Journal abstract)

238740 Hancock, John C. Department of Pharmacology, Louisiana State University Medical Center, New Orleans, LA 70112 **Effect of dextroamphetamine on identified cholinoceptive cells of the snail brain.** Federation Proceedings. 35(3):428, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of dextroamphetamine (D-AMPHET) on identified neurons in the visceral ganglion of Helix Pomatia were reported. Twelve cholinoceptive cells were involved in the study. Seven of the cells were pure cholinergic. Five of the cells responded to D-AMPHET. The action of D-AMPHET was blocked by d-tubocurarine (d-TC), phenoxybenzamine or elevated magnesium. These data indicate that D-AMPHET is acting remotely to affect the cells via synaptic mechanisms. The action of D-

AMPHET was blocked by d-TC but not by phenoxybenzamine or magnesium. On these cells D-AMPHET caused a dose dependent depolarization of the cell membrane. Tolerance to D-AMPHET on cholinoceptive cells appears to involve receptor desensitization. Prior exposure to D-AMPHET prevented the response to nicotine. It is concluded that the action of D-AMPHET in these cells results from a direct action on cholinergic receptors. (Journal abstract modified)

238741 Lytle, Loy D. MIT, Cambridge, MA 02139 **Long term consumption of a tryptophan-poor diet alters the behavioral response to drugs.** Federation Proceedings. 35(3):429, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of long-term consumption of a tryptophan poor diet on behavioral response to drugs was discussed. Results of experimentation suggest that long-term consumption of such a tryptophan poor, corn based diet by rats decreases brain tryptophan and 5-hydroxyindole concentrations and electroshock response thresholds. Rehabilitating corn fed animals by feeding them the corn diets supplemented with tryptophan, or with casein control diets that contain adequate amounts of tryptophan and protein restores brain serotonin and pain response thresholds to normal. Animals consuming the diet deficient in tryptophan showed a potentiated hyperalgesic response following the administration of the tryptophan hydroxylase inhibitor parachlorophenylalanine, or an attenuated analgesic response following the injection of the serotonin uptake blocking drug Lilly 110140 (3-(p-trifluoromethylphenoxy)-N-methyl-3-phenylpropylamine). Futhermore, rats consuming the corn based diet were not analgesic following injections of the opiate narcotic morphine. Results demonstrate that the quality of the diet consumed can influence greatly the behavioral and biochemical potency of drugs. (Journal abstract modified)

238743 Longenecker, Herbert E., Jr.; Deen, H. Gordon; Urschel, Charles W. University of South Alabama, Mobile, AL 36688 **Effects of lithium on neuromuscular transmission.** Federation Proceedings. 25(3):429, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of lithium (Li+) on neuromuscular transmission were reported. Miniature (M) end plate potential (EPP) frequency (F) and amplitude, quantum content (Q) of the EPP, and resting membrane potential (RMP) of Rana Pipiens sartorius muscle were measured, stored and displayed with a computerized intracellular recording system. Following replacement of extracellular sodium by Li+, MEPP amplitude and RMP were unchanged. MEPPF increased to high values then decreased to zero. Total MEPPs recorded after Li represent release of the entire terminal store of transmitter. Initially, Q rose many fold then disappeared over a minute concommittant with high MEPPF long before terminal depletion. EPP block could be caused by failure of nerve terminal action potentials (NTAP) due to severe depolarization, or due to depletion of an immediately releasable pool because of high MEPFF. It was concluded that Li caused depletion of the immediately releasable pool. (Journal abstract modified)

238745 Stokes, Johnes D.; Scudder, Charles L.; Boulos, Badi M. Loyola University Medical Center, Maywood, IL 60608 **An investigation on the dose-response relationship between conventional antioxidant food additives and neurotransmitter metabolism.** Federation Proceedings. 35(3):429, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the dose/response relationship between conventional antioxidant food additives and neurotransmitters in mice was reported. Doses of 5, 50, or 500 mg/kg of either butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) dissolved in peanut oil or peanut oil alone were injected intraperitoneally at specified intervals. Twenty four hours after injection, all doses of BHA were seen to cause large increases whole brain levels of 5-hydroxyindole acetic acid (5HIAA). Insignificant changes, however, were observed in the whole brain levels of serotonin and norepinephrine. Twenty four hours after the injection, all doses of BHT were also shown to cause increases in while brain 5HIAA levels compared with controls. Insignificant changes were observed in the serotonin levels, and there was a tendency to lower whole brain levels of norepinephrine. At shorter intervals, similar results were also found. Findings suggest that the partial serotonin depletion seen in earlier studies was related to an increased serotonin utilization. (Journal abstract modified)

238751 Walker, Charles A.; Soliman, Karam F. A. School of Pharmacy, Florida A and M University, Tallahassee, FL 32307 **Effects of acute ethanol administration on brain biogenic amines.** Federation Proceedings. 35(3):467, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study on the levels of serotonin (5-HT), 5-hydroxyindoleacetic acid acid (5HIAA), norepinephrine (NE) and dopamine (DA) in different regions of the brain in relation to ethanol (ETOH) administration was reported. ETOH produced a marked change in the NE level in the different brain parts studied. Within an hour of ETOH administration, there was at least a four fold increase in the NE level in all brain parts studied. The levels of NE declined again to a comparable level of the control data after 4 hours of ETOH administration. DA levels increased in the different brain parts to reach its maximum level of minimum two folds after 2 hours of ETOH administration. At 4 hours postinjection, the brain dopamine concentration was below the control group. No significant changes were observed in 5-HT or 5HIAA levels except for the cerebellum and the pons where the levels reached its maximum at one hour postinjection. Data suggest that ETOH's effect on the nervous system and the body motor activity might be mediated through its effect on the brain biogenic amines concentration. (Journal abstract modified)

238753 Diaz, Pedro M. University of Miami, Miami, FL 33152 **Inhibition of neuronal serotonin (5-HT) uptake and the anticonvulsant action of trimethadione (TMD).** Federation Proceedings. 35(3):427, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the inhibition of neuronal serotonin (5-HT) uptake and anticonvulsant action of trimethadione (TMD) was reported in rats. Ss were injected before pentylenetetrazol (PTZ) with Lilly 110140 (3-(p-trifluoromethylphenoxy)-n-methyl-3-phenylpropylamine), a drug preventing neuronal uptake of 5-HT. Some rats received para-chlorophenylalanine (PCPA) 70-94 hours before PTZ. All rats received TMD 20 mins. before PTZ. PTZ was given every 10 mins until the tonic extensor component was seen. In rats treated with TMD, the mean convulsant dose (CD50) was increased one hour after Lilly 110140. After TMD and PCPA, the CD50 was increased 6, 12, and 24 hours after Lilly 110140, but was statistically significant at 12 hours only. The data supports the idea that the anticonvulsant action of TMD is partially mediated by serotonergic neurons. (Journal abstract modified)

238758 Bronaugh, R. L.; Ohashi, T.; Goldstein, Menek. Dept. of Psychiatry, Neurochemistry Labs, New York University Medical Center, New York, NY 10016 **The reversal of apomorphine elicited inhibition of synaptosomal tyrosine hydroxylase activity by neuroleptics.** Federation Proceedings. 35(3):485, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the effects of various neuroleptics on apomorphine elicited enzyme inhibition was reported. Several tested neuroleptics reversed maximally the enzyme inhibition by approximately 40%, but the concentration required for maximal reversal differed among them. Using the maximal reversal or 25% reversal as an index of potency, the tested compounds could be ranked in the following order of decreasing potency: (+)butaclamol, fluphenazine, haloperidol, pimozide, chlorpromazine. The potency of some, but not of all, tested drugs to reverse apomorphine elicited enzyme inhibition correlated with their antipsychotic activity in vivo. The interaction of neuroleptics with the presynaptic dopamine receptors may serve as an index of their antipsychotic activity. (Journal abstract modified)

238759 Joh, Tong Hyub; Ross, Robert A.; Reis, Donald J. Dept. of Neurology, Cornell University Medical College, New York, NY 10021 **Rate of biosynthesis of dopamine-beta-hydroxylase in locus coeruleus of rat brain after reserpine.** Federation Proceedings. 35(3):485, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the rate of biosynthesis of dopamine-beta-hydroxylase (DBH) in locus coeruleus (LC) of rat brain after reserpine was reported. Rat brain LCs were removed at various times, and DBH protein was isolated in two ways. The LC was homogenized and incubated with specific antibody to DBH and precipitated; remaining protein was precipitated with TCA. Precipitated DBH was separated by electrophoresis and counted. Purified DBH was added to a 10000 gram supernatant of labeled LC, homogenized in 0.2% triton buffer, separated by disc gel electrophoresis, and counted. In controls, the rate of incorporation of 3H leucine into DBH was 25000 and into remaining protein 68100. Reserpine increased incorporation into DBH by 97%, while into other protein by only 32%. It is concluded that reserpine increases accumulation of DBH in LC by increasing the rate of de novo synthesis of enzyme protein. (Journal abstract modified)

238761 Neff, N. H.; Karoum, F.; Wyatt, R. J. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **The dynamics of dopamine metabolism in various regions of rat brain.** Federation Proceedings. 35(3):486, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the dynamics of dopamine metabolism in various regions of rat brain was reported. Homovanillic acid (HVA) and dihydroxyphenylacetic acid (DOPAC) were measured in seven regions of rat brain by mass fragmentography after injecting pargyline. The steady state ratio of DOPAC to HVA ranged between 1 and 3. After probenecid treatment, HVA increased in all areas where the steady state ratio of DOPAC to HVA was greater than 2. In striatum and cortex, about 2.5times more DOPAC than HVA was formed as compared with midbrain with a value of about 4. In addition, it appeared that more than half of the HBA formed was eliminated by a transport system that was insensitive to probenecid. By injecting pargyline and probenecid together, it was found that only a small fraction of DOPAC was converted to HVA. It is concluded that: DOPAC is the major metabolite of dopamine; probenecid only partially blocks the elimination of the acids from brain; and the pharmacology of neuroleptic drugs should be interpreted with caution if only HVA is analyzed in rats. (Journal abstract modified)

238763 Cerreta, K. V.; Flynn, E. J. Dept. of Pharmacology, CMDNJ, New Jersey Medical School, Newark, NJ 07103 **Passive barbiturate immunity in mice: effect on serum levels and pharmacologic response to administered barbiturates.** Federation Proceedings. 35(3):487, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the effect of serum levels and pharmacologic response on passive barbiturate immunity in mice was reported. Antibodies were produced in rabbits and the sera from these rabbits bound 3H-phenobarbital in vitro; and control rabbit sera did not. The antisera obtained from these actively immunized rabbits was administered intravenously to mice. An antibody binding capacity for 3H-phenobarbital was shown to be sustained in these passively immunized mice for periods of up to 3 weeks. The serum levels of 3H-phenobarbital vs time in passively immunized mice and controls were compared and found to be altered in antibody containing mice. There was a four fold increase in the amount of 3H-phenobarbital present in the serum of passively immunized mice over controls. The higher barbiturate levels were due to binding to a globulin fraction in serum. An altered pharmacologic response to pentobarbital was demonstrated by use of a rotarod apparatus which showed that passively immunized mice were more resistant to ataxia produced by pentobarbital than did controls. This effect was selective for barbiturates and did not modify the ataxia produced by other depressant agents. (Journal abstract modified)

238764 Shah, Nandkumar S.; Hixson, Betsy; Gulati, O. D.; Kuhn, D. Ensor Foundation Research Laboratory, William S. Hall Psychiatric Institute, Columbia, SC 29202 **Placental transfer and maternal and fetal tissue distribution of 14C-methaqualone in mice.** Federation Proceedings. 35(3):488, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of placental transfer and maternal and fetal tissue distribution of 14C-methaqualone (MTQ) in mice was reported. The concentration of unchanged MTQ in several maternal and a few fetal organs was examined 90 minutes, 3, 6 and 24 hours later. In both maternal and fetal tissues, peak concentrations of MTQ were reached 90 minutes after its administration. The highest concentration was found in the fat followed by the uterus, plasma, liver, muscle, lung, placenta, spleen, heart, spinal cord, kidney, brain, amniotic fluid and eye. At 90 minutes, the fetal whole brain level of MTQ was only 50% the maternal brain level, but at 3 hours the differences were insignificant as a result of a decrease in the maternal and some increase in fetal tissue levels. In three fetal brain areas (cerebellum, cerebrum and brainstem) the levels were identical at 90 minutes; however, the level in the cerebellum declined somewhat rapidly reaching that in the cerebrum at 6 hours. Levels at MTQ in maternal and fetal tissues were considerably lower at 24 hours. (Journal abstract modified)

238765 Karbowski, M.; Jagoda, A.; Johnson, K.; Dewey, W. L.; Harris, L. S. Dept. of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **The effect of delta9-THC on high and low affinity uptake of choline and its relationship to**

turnover of acetylcholine in mouse brain. Federation Proceedings. 35(3):506, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the effect of delta9-tetrahydrocannabinol (THC) on turnover of acetylcholine in mouse brain was reported. A high affinity (HA) transport mechanism exists for choline (Ch) which is specific for cholinergic neurons and results in a high percent of conversion to acetylcholine (ACh); a low affinity (LA) transport system is believed to be a nonspecific property of membranes in general. THC stimulated the HA uptake at 3, 10 and 30, but not 100mg/kg (119%, 124%, 131%, and 108% of control, respectively). The LA uptake system was not significantly affected. THC depressed the turnover rate of ACh (68%). The data suggests that low doses of THC facilitate the uptake of the specific pool of Ch that is responsible for ACh synthesis, while at high doses (100mg/kg), the uptake is not stimulated, and turnover rate of ACh is depressed. (Journal abstract modified)

238766 Abel, Ernest L.; Siemens, Albert J. Research Institute on Alcoholism, Buffalo, NY 14203 **Response to delta9-tetrahydrocannabinol, barbiturates and ethanol in lactating, virgin female, and male mice.** Federation Proceedings. 35(3):506, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the responsiveness of lactating, virgin female and male mice to depressant drugs was reported. Locomotor activity in the open-field was depressed in lactating mice relative to males and virgin females in response to delta9-tetrahydrocannabinol (THC), but was increased in response to pentobarbital. Both drugs are metabolized by the hepatic mixed function oxidase system. No differences were observed in the locomotor response of the three groups to ethanol (metabolized by alcohol dehydrogenase). THC produced a significant elevation of body temperature in males with other groups exhibiting no increase. At 10mg/kg of THC, the body temperature of lactating mice was decreased significantly compared to virgin females and males. No differences occurred between the groups in the effect of ethanol on body temperature. Also, no differences were observed in sleep time in response to ethanol or to thiopental. However, fewer lactating mice lost their righting reflex at 30mg/kg pentobarbital. These results demonstrate that lactating females exhibit modified drug effects which may in part be due to changes in drug metabolizing systems associated with lactation. (Journal abstract modified)

238767 Smiley, K. A.; Karler, R.; Turkanis, S. A. Dept. of Pharmacology, University of Utah College of Medicine, Salt Lake City, UT 84132 **Effects of cannabinoids on the in-vitro perfused rat heart.** Federation Proceedings. 35(3):506, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the chronotropic and inotropic effects of four naturally occurring cannabinoids examined with a Langendoriff preparation was reported. The cannabinoids exhibited various effects on cardiac rate: delta9-tetrahydrocannabinol (THC) and cannabinol produced an increase; cannabidiol (CBD) caused a decrease; and delta9-THC induced arrythmias. Furthermore, all the cannabinoids markedly depressed the force of contraction. The results of additional experiments with delta9-THC and 3H-CBD indicate that the drugs accumulate in the heart; consequently, the observed cardiac effects are associated with tissue concentrations much greater than those of the perfusion medium. The findings demonstrate that the cannabinoids can produce cardiac effects independently of their central nervous system actions. The observed effects, however, occur at very high tissue concentrations, resulting from the extraction of the drugs from the perfusion medium. (Journal abstract modified)

238769 Bloom, A. S.; Johnson, K. M.; Bowman, F. J.; Dewey, W. L. Dept. of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Correlation between the effects of several cannabinoids on catecholamine synthesis, body temperature, and behavior.** Federation Proceedings. 35(3):506, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of possible correlations between the effects of several cannabinoids on catecholamine synthesis, body temperature, and behavior was reported. Delta9-tetrahydrocannabinol (THC) at doses of 3, 10, 30 and 100mg/kg caused significant increases in the accumulation of newly synthesized dopamine (DA) and in the accumulation of newly synthesized norepinephrine (NE), as well as decreases in body temperature. Three and 10mg/kg but not higher doses of both 11-hydroxy-THC and HHC produced larger increases in the accumulation of newly synthesized DA and decreases in body temperature than the same doses of THC. There was no difference in the effects of the three cannabinoids on the increase in NE synthesis. Cannabidiol, cannabinol, and HHC did not alter catecholamine synthesis or body temperature. Results indicate that behaviorally active cannabinoids produce both increased activity in catecholamine containing neurons and hypothermia in the mouse, while those cannabinoids with little behavioral activity also had little effect on these parameters. (Journal abstract modified)

238770 Rosenberg, Howard C.; Okamoto, Michiko. Dept. of Pharmacology, Cornell University Medical College, New York, NY 10021 **Loss of inhibition in spinal cord during barbiturate withdrawal.** Federation Proceedings. 35(3):507, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study on loss of inhibition in spinal cord during barbiturate withdrawal was reported. Cats were prepared for studies of inhibition and facilitation of segmental spinal reflex activity at the peak of withdrawal. Under volatile anesthesia the neuraxis was sectioned at C-1, both carotid arteries were ligated, and artificial respiration was begun. The lumbar cord was exposed and peripheral nerves of one hindlimb were prepared for stimulation. Action potentials were recorded from ipsilateral ventral roots L-7 and S-1 that had been cut near to their exit through the dura mater. Recurrent (Renshaw cell mediated) inhibition, which was very reproducible in untreated cats, was almost totally absent during withdrawal. Presynaptic inhibition was also decreased during withdrawal. These findings indicate that loss of activity in inhibitory pathways may play a central role in the overall barbiturate withdrawal syndrome. (Journal abstract modified)

238771 Amicarella-Boyle, Richard; Polosa, Canio. Dept. of Physiology, McGill University, Montreal, Quebec, Canada **An investigation on the effects of L-dopa and 5-HTP on sympathetic preganglionic neurones.** Federation Proceedings. 35(3):509, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the effects of L-dopa and 5-hydroxytryptophan on sympathetic preganglionic neurons was reported. L-Dopa and 5-hydroxytryptophan (5-HTP), administered in cats either spinalized at C1-C6 or with intact neuraxes but baroreceptor denervated, produced long-term inhibition of spontaneous sympathetic preganglionic (SPN) activity. The inhibitory action of 5-HTP was prevented

by pretreatment with central decarboxylase inhibitors. D-dopa did not influence SPN activity. Prior administration of a peripherally acting decarboxylase inhibitor did not alter the actions of L-dopa and 5-HTP. Alpha-adrenergic blockage neither prevented nor reversed the effect of L-dopa or 5-HTP. A 5-hydroxytryptamine (5-HT) receptor antagonist blocked the action of 5-HTP. It is suggested that L-dopa and 5-HTP must be converted enzymatically to noradrenaline and 5-HT, respectively, by central mechanisms in order to inhibit SPN activity. The action of L-dopa does not appear to be mediated by a conventional alpha-receptor, while receptor antagonism has been demonstrated for 5-HT. (Journal abstract modified)

238772 Sharpe, L. G.; Pickworth, W. B. NIDA Addiction Research Center, Lexington, KY 40511 **Central action of amphetamine-induced mydriasis in the dog.** Federation Proceedings. 35(3):509, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the central action of amphetamine induced mydriasis in the dog was reported. The left superior cervical ganglia were removed in six dogs. Beginning 30 days postoperatively, epinephrine (E) and d-amphetamine (A) were infused i.v. for 10 minutes following either saline, phenoxybenzamine (PBZ) or haloperidol (H). Pupils and nictitating membranes were measured photographically. E dilated the pupil and retracted the nictitating membrane only on the denervated side, while A dilated both pupils and retracted both nictitating mebranes. PBZ constricted the innervated but not the denervated pupil, completely antagonized E, but only partially antagonized A. H constricted both pupils and was more effective in antagonizing A than PBZ. In addition, the stereotypic activity (head movements) produced by A was antagonized by H, but not by PBZ. A was also studied in 20 unanesthetized decerebrate dogs and produced more mydriasis in the midpontine postcollicular than in the midcollicular dog. These results suggest that A produces mydriasis in the dog through both peripheral sympathetic mechanisms and a central mechanism involving inhibition of the oculomotor nucleus which may involve dopamine. (Journal abstract modified)

238773 Ciaramitaro, D. A.; Hruska, R. E.; Yamamura, H. I.; Huxtable, R. J. Dept. of Pharmacology, University of Arizona Medical Center, Tuscon, AZ 85724 **Purification of (3H)taurine of high specific activity.** Federation Proceedings. 35(3):522, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the neurotransmitter properties of taurine (TAU) was reported. Exchange tritiation of TAU produced radioactive contaminants which were not separable from TAU by ion exchange chromatography and which can lead to inaccurate estimates of purity. Isotopic dilution analysis indicated that TAU was only 71% radiochemically pure. The radiochemical impurities were not volatile, not removable by extraction with organic solvents, and did not separate on an anion exchange column under a chloride gradient. Partial purification to 85% was achieved by the boiling of an aqueous solution for 30 seconds and the addition of hydrogen peroxide and 2.5% ammonium molybdate. This procedure removes hypotaurine and thiotaurine possibly formed under the tritiation conditions. Column chromatography of the product yielded TAU of 90% purity. (Journal abstract modified)

238777 Tjioe, Sarah A.; Manian, Albert A.; O'Neill, John J. Department of Pharmacology, Ohio State University, Columbus, OH 43210 **Effects of B-hydroxylated phenothiazine derivatives on isolated brain mitochondria.** Federation Proceedings. 35(3):543, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of beta-hydroxy-chlorpromazine (B-OH-CPZ), B-OH-7,8-diOH-CPZ, and B-OH-7,8-dioxo-CPZ on isolated rat brain mitochondria were reported. B-OH-7,8-diOH-CPZ and B-OH-dioxo-CPZ permit adenosine triphosphate supported calcium uptake to proceed for 2 minutes but then cause calcium to be released from the mitochondria. The calcium efflux reaches completion in about 6 minutes. These results are similar to those previously reported for 7,8-diOH-CPZ. B-OH-CPZ, however, had no effect in this system. B-OH-7,8-diOH-CPZ, B-OH-7,8-dioxo-CPZ and B-OH-CPZ all cause a slight initial increase in the rate of respiration with glutamate as substrate. The block of state III respiration by B-OH-CPZ was less complete than that observed with the other two beta-hydroxylated compounds. These effects on respiration are accompanied by a depression of ATP synthesis. Results indicate that B-OH substitution enhances the inhibitory effects of CPZ on mitochondrial respiration but not on calcium retention. B-OH substitution causes only slight changes in the effects of 7,8-diOH-CPZ in these systems. (Journal abstract modified)

238779 Olsen, Richard W. University of California, Riverside, CA 92502 **Effects of tranquilizer drugs on GABA release in vitro.** Federation Proceedings. 35(3):543, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of tranquilizer drugs on gamma-aminobutyric acid (GABA) release in vitro were reported. Diazepam increased significantly the calcium ion stimulated release of (14C)GABA from mouse brain cortex fractions enriched in synaptosomes. Other compounds which increased GABA release were 2,4-diaminobutyrate, nipecotic acid, and (nonradioactive) GABA itself, all potent competitive inhibitors of GABA transport by synaptosomes. This stimulation of release probably reflects increased exchange of GABA via the transport system rather than actual nerve ending secretory relase. Diazepam inhibited uptake of GABA by synaptosomes, and might therefore, like the GABA analogues, stimulate reverse transport of GABA from nerves or glia. This could potentiate GABA mediated inhibitory activity in the nervous systems. Nonspecific inhibitors of GABA transport such as imipramine, chlorpromazine, and haloperidol did not stimulate GABA release but potently inhibited the calcium ion stimulated release from synaptosomes. (Journal abstract modified)

238782 Jung, M.; Lippert, B.; Metcalf, B.; Rieger, B.; Sjoerdsma, A. Centre de Recherche Merrell International, Strasbourg, France **A comparison of the biochemical effect of two catalytic inhibitors of mammalian brain GABA-transaminase: gamma-vinyl-GABA (amino-4-hex-5-enoic acid) and gamma-acetylenic GABA (amino-4-hex-5-ynoic acid).** Federation Proceedings. 35(3):544, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a comparison of the biochemical effect of two catalytic inhibitors of mammalian brain gamma-aminobutyric acid transaminase (GABA-T) was reported. Both gamma-vinyl GABA and gamma-acetylenic-GABA inhibit mammalian brain GABA-T (pig, rat, mouse) in a time dependent, irreversible manner. Acetylenic GABA is about equipotent on all these enzymes. Both compounds are over 100 times more potent against GABA-T than against aspartate or alanine transaminase. Of greater importance is the

fact that gamma-vinyl GABA has no effect on glutamic acid decarboxylase (GAD) in vitro while gamma-acetylenic GABA inhibits this enzyme irreversibly. The acetylenic derivative, nevertheless, is about 30 times more potent in inhibiting GABA-T than GAD. Both compounds, when given to rats or mice by a peripheral route produce a dose dependent decrease of whole brain GABA-T activity and increase of brain GABA levels. In vivo, gamma-vinyl GABA is also more selective than gamma-acetylenic GABA, producing no concomitant decrease of GAD activity. (Journal abstract modified)

238783 Messing, Rita B.; Fisher, Laurel A.; Phebus, Lee. MIT, Cambridge, MA 02139 **Injections of amino acids that alter brain serotonin increase the sensitivity to electroshock in rats.** Federation Proceedings. 35(3):544, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of amino acids on brain serotonin and sensitivity to electroshock in rats were reported. Rats injected with valine, phenylalanine, or leucine have reduced concentrations of brain tryptophan and the 5-hydroxyindoles. These animals also appear to be hyperalgesic to presentations of electric shock, inasmuch as the mean shock intensities necessary to elicit a jump response in animals injected with l-valine, leucine, or phenylalanine were 65%, 81%, and 81%, respectively, of the jump response thresholds of vehicle treated rats. These data add further support for the hypothesis that brain serotonin constraining neurons may normally mediate the response to painful stimuli. (Journal abstract modified)

238784 Mishra, R. K.; Hollett, C. R. Department of Pharmacology, Meharry Medical College, Nashville, TN 37208 **CNS transmitters and the hypothalamus.** Federation Proceedings. 35(3):544, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the relationship between central nervous system transmitters and the hypothalamus was discussed. Two substances were isolated from the dog hypothalamus; one promoted free fatty acid (FFA) mobilization (LM) in vivo and in vitro; the second inhibited norepinephrine (NE) induced FFA release from adipose tissue slices, and in the intact animal suppressed the rise in plasma FFA associated with NE. Under conditions of crowding LM caused a 44% reduction in brain NE; this action was without behavioral changes seen with amphetamine, which decreased brain NE 15%. Unlike amphetamine, crowding was not a factor in LM action. Neither amphetamine nor LM alone produced significant changes in brain dopamine (DA); however, simultaneous administration of both agents produced a synergistic effect; brain DA was increased 50%. (Journal abstract modified)

238789 Blum, Kenneth; Feinglass, Sanford J.; Briggs, Arthur H.; Wallace, Jack E. University of Texas Health Science Center, San Antonio, TX 78284 **Amphetamine-induced polyphasic morbidity: studies on strain differences, polydrug effects and mechanism.** Federation Proceedings. 35(3):563, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, amphetamine (AMP) induced polyphasic morbidity in mice was reported. Strain D turned an activity wheel 17 times and 3.5mg/kg was required to reach the first mortality peak whereas strain H turned an activity wheel 45 times and 12.5gm/kg was necessary to reach the first mortality peak. Delta9-tetrahydrocannabinol (THC) reduced mortality by 50%. Ethanol at 3mg/kg i.p. reduced mortality by 100% and at 0.75g/kg reduced it by 50%. Pentobarbital unexpectedly produced a marked potentiation of AMP toxicity, whereas morphine, methadone and naloxone had no significant effect. L-Dopa resulted in enhancement of the response whereas the dopamine receptor blocker pimazide completely blocked AMP toxicity. Methysergide, the serotonergic blocker, also significantly inhibited morbidity. Propranolol, the beta blocker, and phentolamine both significantly blocked AMP induced toxicity. It is suggested that dopamine may be the central mediator whereas epinephrine or norepinephrine may mediate the peripheral component of AMP induced toxicity. (Journal abstract modified)

238790 Morgan, W. W.; Huffman, R. D. University of Texas Health Science Center, San Antonio, TX 78284 **Effect of chronic barbital administration and subsequent withdrawal on catecholamine content and turnover in rat brain.** Federation Proceedings. 35(3):563, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of chronic barbital administration and withdrawal on catecholamine content and turnover in rat brain were reported. Barbital was administered chronically for 5 weeks in increasing concentrations in saccharine treated drinking water to male rats. At the termination of the drug regimen, rats were sacrificed at 0, 24 or 48 hours following barbital withdrawal. Spontaneous convulsions, irritability and weight loss observed during the withdrawal period provided evidence that the rats were barbital dependent. Dopamine (DA) content in the telencephalone was significantly decreased 48 hours following barbital withdrawal. No significant change in noradrenaline (NA) content was observed in either the telencephalon or the brainstem. However, at 24 and 48 hours following barbital withdrawal, the depletion of NA observed 2 hours following the intraperitoneal administration of alpha-methyl-para-tyrosine was significantly greater in both the telencephalone and brainstem of barbital dependent rats. These data suggest that NA turnover is increased following withdrawal of barbital dependent rats. It is suggested that the increased irritability and convulsion susceptibility observed during barbital withdrawal may be the result of this increase in NA turnover or the decrease in DA content in the brain. (Journal abstract modidied)

238791 Tzeng, S. F.; Ho, I. K. Department of Pharmacology & Toxicology, University of Mississippi Medical Center, Jackson, MS 39216 **Effects of acute and chronic pentobarbital administration on brain gamma-aminobutyrate (GABA) and glutamate (GLU) levels in the mouse.** Federation Proceedings. 35(3):564, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of acute and chronic pentobarbital administration on mouse brain gamma-aminobutyric acid (GABA) and glutamate (glu) were reported. Male mice after receiving an administration of sodium pentobarbital, demonstrated a 15% increase in brain GABA level and a 22% decrease in Glu level as compared to those of the control group. There was a small but significant increase in Glu decarboxylase (GAD) activity simultaneously. To monitor both GABA and Glu levels during the development of tolerance to pentobarbital, animals were rendered tolerant by implanting a specially formulated 75mg pentobarbital (acid form) pellet for the maximum of 72 hours. The control group received a placebo pellet for a same period of time. At 4 hr after pentobarbital pellet implantation, a 19% and 27% decrease in brain GABA and Glu were measured, respectively. At both 24 and 72 hr after pellet implantion, GABA levels were 8% and Glu levels were 5% significantly lower than those

of the control. The GAD activity in pentobarbital pellet implanted group was also inhibited more than 25%. It was suggested that the action of pentobarbital may be mediated by changes in the function of GABA system in the central nervous system. (Journal abstract modified)

238792 Cohn, M. L.; Wolfson, S. K., Jr.; Steichen, F. M.; Cohn, M. University of Pittsburgh School of Medicine, Pittsburgh, PA 15213 **Thyrotropin releasing hormone (TRH) an antidote to amobarbital overdosage in the rhesus monkey.** Federation Proceedings. 35(3):564, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the use of thyrotropin releasing hormone (TRH) as an antidote to amobarbital overdosage in the rhesus monkey was reported. TRH was given and its effectiveness was compared to that of dibutyryl cyclic adenosine monophosphate (AMP). Stable vital signs for one hour were followed by injection of 155mg/kg of amobarbital i.p.,a lethal dose. In control animals, the mean arterial blood pressure (MABP) fell to 50% of initial values within 5-10 .in and death occurred within 30 min. Dibutyryl cyclic AMP, injected after MABP fell 50% of control values, stabilized MABP within 2-3 min. MABP returned to control values within 2 hours. In contrast, TRH was less effective in reversing shock and recovery of MABP required upwards of 6 hours. TRH injected prior to onset of shock prevented fall in MABP. The findings suggest that while TRH may be useful in treatment of overdosage before onset of shock, dibutyryl cyclic AMP is a more effective antidote to drug overdosage. (Journal abstract modified)

238795 Giedt, W. Reid, Jr.; Winters, Wallace D. University of California, Davis, CA 95616 **Pharmacological stimulation of the pineal: potentiation of ketamine response in the chick.** Federation Proceedings. 35(3):564, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the potentiation of ketamine (K) response in the chick through pharmacological stimulation of the pineal was reported. The influence of isoproterenol (ISP), norepinephrine (NE) and dopamine (DA) on K action was examined in the chick whose blood brain barrier is immature to bioamines. Chicks were maintained on 12 hour light/dark cycles. ISP, NE or DA administered 60 minutes before K produced a significant increase in K action. Pinealectomy abolished the catecholamine induced K augmentation. These results indicate that 1) catecholamines potentiate K response after a 60 minute lag period, and 2) the pineal gland is involved in this potentiation.

238798 Creveling, C. R.; Ghosh, P.; Dismukes, R. K.; Daly, J. NIH, Bethesda, MD 20014 **Central depletion of norepinephrine in guinea pig: lack of effect on norepinephrine-sensitive cyclic AMP-generating systems.** Federation Proceedings. 35(3):609, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effect of cyclic adenosine monophosphate (cAMP) on central depletion of norepinephrine in the guinea-pig was reported. Levels of norepinephrine in the cerebral cortex are reduced to similar extents in rat and guinea pigs after intraventricular administration of 6-hydroxydopamine, intraperitoneal administrative of reserpine or lesions of the medial forebrain bundle. In rat, interference with noradrenergic input by these pretreatments leads to enhanced responsiveness of the norepinephrine sensitive cyclic AMP generating systems of cerebral cortical brain slices. In guinea-pig, the responsiveness of cortical cyclic AMP systems to norepinephrine, serotonin and histamine is unaltered. Adenosine sensitive cyclic AMP systems become hyperresponsive after reserpine. The reasons for lack of adaptation of norepinephrine sensitive cyclic AMP systems in guinea-pig cerebral cortex are not clear. It is suggested that lower levels of norepinephrine in guinea-pig compared to rat might reflect a lower functional activity of noradrenergic pathways in the former species. As a result of low functional input the postsynaptic cyclic AMP systems might already be maximally responsive. (Journal abstract modified)

238806 Sullivan, M. F.; Willard, D. H. Battelle-Northwest, Richland, WA 99352 **The effect of chronic marihuana smoking on the beagle dog.** Federation Proceedings. 35(3):643, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the long-term effects of marihuana in dogs was reported. Dogs were exposed to marihuana smoke by a system designed to simulate human smoking habits. The animals smoked up to 13 cigarettes daily for 18 months. During that time, measurements were made of their smoking efficiency, venous carboxyhemoglobin levels, respiration and heartrates, neurologic functions, blood cell counts and blood chemistry. After cigarettes labeled with 3H-delta9-tetrahydrocannabinol (THC) were smoked, quantitation of the tritium activity in the excreta, blood and expired smoke indicated that the daily dose of THC was about 2mg/kg. The carboxyhemoglobin levels increased three fold in both marihuana and placebo smokers. Both heart and respiration rates decreased with each succeeding marijuana cigarette. Tolerance developed to the bradycardia after 1 year of marihuana administration. The dogs showed neurologic decrements and ataxia after exposure to marihuana at the end of each smoking day. No other measurable impairments were noted throughout the study, nor was any pathologic effect found when the dogs were necropside at the termination of the study. (Journal abstract modified)

238808 Warner, W.; Carchman, R. A.; Harris, L. S.; Watts, D. T. Department of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Inhibition of corticosteroidogenesis by cannabinoids.** Federation Proceedings. 35(3):643, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the inhibition in mice of corticosteroidogenesis by cannibinoids was reported. Steroidogenesis induced by cholera toxin or cyclic adenosine monophosphate (CAMP) were similarily inhibited, suggesting that the site of cannabinoid action is subsequent to the generation of CAMP. Inhibition of steroidogenesis by delta9-tetrahydrocannabinol (THC) was also seen in normal cat adrenal cell suspensions. Effects on steroidogenesis was dissociated from behavioral and antitumor activity by the activities of cannabinol and cannabidiol respectively. A concentration (THC) which caused a significant inhibition of steroidogenesis failed to inhibit macromolecular synthesis (incorporation of thymidine and animo acids into TCA precipitates) in Y-1 cells. THC inhibited Y-1 oxygen consumption but did not exhibit the dose dependency demonstrated by its effects on steroidogenesis. These data argue against general depression of cell function as the sole mechanism of inhibition of corticosteroidogenesis. (Journal abstract modified)

238809 Earnhardt, J. T.; Adams, M. D. Department of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Mechanism of vasoconstrictor action of delta9-tetrahydrocannabinol in pithed and anesthetized rats.** Federation Proceedings. 35(3):643, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the cardiovascular effects in rats of delta9-tetrahydrocannabinol (THC) were reported. In the anesthetized rat, hypotension and bradycardia followed the initial increase in blood pressure. There was no hypotension or bradycardia produced in the pithed animal by THC at doses up to 3.0mg/kg. The magnitude of the transient pressor response was greater in the anesthetized animal than in the pithed animal. In a dose which reduced the pressor response to intravenous norepinephrine at least 80%, phentolamine reduced the pressor response to intravenous THC more than 50% in the anesthetized animal. The reduction of the pressor response with phentolamine pretreatment in the pithed animal was 30% at 1.0mg/kg. The response to intravenous norepinephrine was enhanced in the pithed animal after THC administration. The data suggest that intravenous THC produces vasoconstriction which is mediated in part through adrenergic mechanisms. (Journal abstract modified)

238810 Jandhyala, B. S.; Malloy, K. P.; Buckley, J. P. Division of Cardiovascular Research, College of Pharmacy, University of Houston, Houston, TX 77004 **Chronic cardiovascular effects of delta9-tetrahydrocannabinol (delta9-THC) in the mongrel dogs.** Federation Proceedings. 35(3):643, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the cardiovascular effects of delta9-tetrahydrocannabinol (THC) in mongrel dogs were reported. A slight increase in the heartrate noted in the treated group was not significant from that of the placebo group. Following the administration of pentobarbital there was a marked increase in the heartrate of the both groups; but the increase in the placebo (102%) was significantly greater than that occurring in the treated group (38%). Since peripheral autonomic function was not altered in the THC treated group, the low heartrate level in the treated group under anesthesia was due to the ability of chronic THC to antagonize the effects of pentobarbital. Further, chronic THC did not produce any significant alterations either in various hemodynamic parameters or in the autonomic receptor activity. Pressure flow curves of the perfused hind limb suggested that there was a significant reduction in the intrinsic tone of the vascular smooth muscle. The data demonstrate that certain effects of THC administered for 7 days differed both qualitatively and quantitatively from those noted following a single injection. (Journal abstract modified)

238812 Olmsted, C. A.; Lee, G. M. Department of Biological Science, University of New Orleans, New Orleans, LA 70122 **Brain synaptic membrane NaK-ATPase following chronic injection of delta9-tetrahydrocannabinol (THC).** Federation Proceedings. 35(3):644, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of chronic injection of delta9-tetrahydrocannabinol (THC) on brain synaptic membrane sodium and potassium activated adenosine triphosphatase (Nak-ATPase) were reported. In vivo injection of THC to rats resulted in 28% and 64% inhibition of brain synaptic membrane NaK-ATPase. The hypothesis that fat stored cannabinoids might be remobilized during fasting was tested. Brain synaptic membrane NaK-ATPase was used as indicator for such remobilization. In three experiments, injections of 2mg/kg per day for 5 days were given to each of 20 rats. Twenty-four hours prior to obtaining brain synaptic membranes, 10 of the rats were fasted, and the other 10 were continued on ad lib feeding. Under these conditions, it does not appear that residual THC is remobilized in sufficient quantity to affect the brain synaptic membrane Nak-ATPase. However, it was suggested that higher dosages of THC, or longer periods of fasting, may show some effect. (Journal abstract modified)

238815 McConnell, W. R.; Borzelleca, J. F.; Dewey, W. L. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **The mechanism by which delta9-tetrahydrocannabinol (THC) produces a decrease in salivary flow following electrical stimulation.** Federation Proceedings. 35(3):644, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the mechanism by which delta9-tetrahydrocannabinol (THC) produces a decrease in salivary flow following electrical stimulation was reported. THC produced a 45% decrease in submaxillary gland arterial blood flow in dogs. This paralleled the decrease (50%) in salivary flow. Neither 0.5nor 1.0mg/kg produced a significant change in the activity of cholinesterase in saliva or blood of cats and dogs. THC lowered the acetylcholine (Ach) content of the bath fluid following electrical stimulation of the guinea-pig ileum. It appears that THC may be acting on Ach presynaptically in salivary tissue. Therefore, THC may be producing a decrease in salivary flow following electrical stimulation by decreasing the effective levels of Ach necessary for effector cell stimulation. The decrease in blood flow is a contributing factor. (Journal abstract modified)

238816 White, A.; Carchman, R. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Cellular mediated decreases in sensitivity to the inhibitory effects of delta9-tetrahydrocannabinol (delta9-THC).** Federation Proceedings. 35(3):644, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, cellular mediated decreases in sensitivity to the inhibitory effects of delta9-tetrahydrocannabinol (THC) were reported in mice. It was noted that mice bearing the Lewis lung adenocarcinoma develop a resistance to the antitumor properties of THC. This resistance is not host mediated. Tissue culture experiments demonstrate that the resistance may be tumor related. Cells were either continuously exposed (CE) to delta9-THC or acutely exposed (AE) for 2.25 hrs. The doubling time of CE cells was increased from 18 to 28 hours. Acute exposure to THC decreased the incorporation of 3H-thymidine (3H-Tdr) into acid precipitable counts 59% as compared to 39% in CE cells. This represents a decrease of 2% in counts/mg protein by CE cells and 59% by AE cells compared to ethanol controls. In subsequent experiments CE cells were pulsed with THC for 2 hours. This increase in drug concentration did not affect the incorporation of 3H-Tdr by CE cells but reduced incorporation by AE cells from 50% control to 5%. It is concluded that CE cells exhibit significantly less inhibition of macromolecular deoxyribonucleic acid (DNA) synthesis than AE cells. (Journal abstract modified)

238820 Maple, P. J.; Borison, R. L.: Sabelli, H. C. Chicago Medical School, Chicago, IL 60612 **Possible mediation of the euphoriant and sedative effect of marihuana by 2-phenylethylamine and by phenylacetic acid.** Federation Proceedings. 35(3):668, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the mediation of the euphoriant and sedative effects of tetrahydrocannabinol (THC) by 2-phenylethylamine (PEA) and phenylacetic acid were reported. It was noted that pretreatment with a wide variety of monoamine oxidase (MAO) inhibitors prevents the sedative ef-

fects of THC in mice. Since behavioral sedation is produced by the deaminated metabolites of biogenic amines, their synthesis may underlie the sedative actions of THC. Following the intraventricular injection of PEA-1-14C, a 160% greater conversion to phenylacetic acid (PAC) after THC than in control rabbits was found. THC must inhibit a major metabolic route other than MAO. It was suggested that the euphoriant effects of THC may be partially mediated by brain PEA, whereas its sedative effects may depend on the formation of its deaminated metabolites. (Journal abstract modified)

238822 Crowley, William R.; Rodriguez-Sierra, Jorge F.; Komisaruk, Barry R. Institute of Animal Behavior, Rutgers University, Newark, NJ 07102 **Analgesic effect of vaginal stimulation in rats: modulation by catecholamines and steroids.** Federation Proceedings. 35(3):668, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the analgesic effect of vaginal stimulation in rats was reported. It was found that probing against the vaginal cervix with a glass rod markedly increased the electric current intensity needed to induce vocalization to tail shock (vocalization threshold). As the force exerted against the cervix was increased progressively, the vocalization threshold increased progressively. Pretreatment with estradiol benzoate potentiated the analgesic effect of cervical stimulation. Progesterone had no effect when given alone, but prevented the estradiol induced potentiation. Pharmacological manipulations included: the analgesic effect of cervical stimulation was significantly potentiated by norepinephrine (NE) receptor stimulation by clonidine; dopamine (DA) receptor blockade by pimozide (1 mg/kg, 3 hr). The analgesic effect of cervical stimulation was significantly reduced by inhibition of NE synthesis by alpha-methyltyrosine or disulfiram, by blockade of NE receptors with phentolamine, by peripheral depletion of NE with 6-hydroxydopamine, and by DA receptor stimulation with apomorphine. (Journal abstract modified)

238823 Morzorati, S. L.; Barnes, C. D. Indiana State University, Terre Haute, IN 47809 **Iontophoretic application of antagonists to putative transmitters on vestibular units involved in a specific inhibitory interaction.** Federation Proceedings. 35(3):668, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of antagonists to putative transmitters on vestibular units involved in a specific inhibitory interaction were reported. An inhibitory convergence from branches of the VIIIth nerve onto vestibular neurons was specifically investigated. Most units were identified as second order neurons. Iontophoretic application of antagonists to cholinergic, glycinergic and adrenergic systems was employed in hopes of determining the specific inhibitory transmitter. Although the antagonists tried did not seem to have a direct effect on the inhibition in question, they influenced the system indirectly. Systemic injections of the same drugs substantiate this conclusion. It appears that the transmitter involved in this specific vestibular inhibition is not one of the commonly accepted transmitters, or alternatively that an uncommon receptor is involved. (Journal abstract modified)

238825 Corson, Samuel A.; Corson, E. O'Leary; Arnold, L. Eugene. Department of Psychiatry, Ohio State University, Columbus, OH 43210 **Dose-response studies on effects of amphetamine on activity and oxygen consumption in dog and cat models of hyperkinesis (hypoinhibitory syndrome).** Federation Proceedings. 35(3):669, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of amphetamine on activity and oxygen consumption in dog and cat models of hyperkinesis (hypoinhibitory syndrome) were reported. The beneficial normalizing effects in hyperkinetic dogs and cats were obtained within a narrow dose range, higher dosages producing hyperactivity, stereotype, and disorientation comparable to effects of amphetamine on normal dogs. Within the same normalizing dosage range, amphetamine decreased oxygen consumption, with higher dosages leading to increased oxygen consumption. These dose response effects lend support to the hypothesis that the primary defect in hyperkinetic animals and children may be related to a deficiency in catecholamine neurotransmitters in inhibitory brain systems. The beneficial effects of low doses of amphetamine are thus not paradoxical but normalizing by supplying the needed neurotransmitters. Higher dosages fail to normalize by flooding synaptic areas with released catecholamines. Further research is recommended. (Journal abstract modified)

238826 Schmidt, Richard H.; Roskoski, Robert, Jr.; Bhatnagar, Ranbir K. Department of Pharmacology, University of Iowa, Iowa City, IA 52242 **6-Hydroxydopamine (6-OHDA) administration to neonatal rats fails to affect the development of tyrosine hydroxylase (TH), choline acetyltransferase (CAT) and glutamic acid decarboxylase (GAD) in the CNS.** Federation Proceedings. 35(3):669, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effect of 6-hydroxydopamine (6-OHDA) on the development of tyrosine hydroxylase (TH), choline acteyltransferase (CAT) and glutamic acid decarboxylase (GAD) in the central nervous system were reported. 6-OHDA prevented full development of the activities of TH and CAT in the superior cervical ganglion. However, the development of the activities of CAT, GAD, and TH was not altered in any of the brain areas. Vmax and Km of regional TH with respect to tyrosine did not differ from controls. Unilateral electrolytic lesions in the area of the locus coeruleus of adult rats following neonatal administration of 6-OHDA reduced the TH activity of the telencephalon to 70% as compared with the control side. Thus it appears that the development of telencephalic CAT and GAD is not contingent upon normal levels of NE during the major period of maturation. In addition it appears that complete degeneration of telencephalic NE nerve terminals does not occur with the 6-OHDA treatment employed. (Journal abstract modified)

238828 Jenden, Donald J.; Parker, Thomas; Roch, Margareth; Macri, James; Fainman, Francine. Department of Pharmacology, UCLA School of Medicine, Los Angeles, CA 90024 **Some pharmacological properties of cyclocholine, a reactive analog of choline.** Federation Proceedings. 35(3):697, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the pharmacological properties of N-methyl,N-(2-hydroxyethyl)aziridinium p-toluenesulfonate (cyclocholine: CCh) and N-(2-chlorethyl),N-2-hydroxyethyl,N-methylamine hydrochloride (HCl) (choline mustard: ChM) were reported. It was noted that their actions are similar, and that ChM is presumably converted spontaneously to the more active CCH in aqueous solution. The prolonged duration of action is further substantiated by considerably greater sensitivity to the drug when administered a second time following a 24 hr interval. The rat phrenic nerve diaphragm preparation shows dose dependent neuromuscular block which is inhibited but not reversed by choline (Ch); CCh produces a similar inhibited by Ch or hemicholinium-3. It was

suggested that CCh acts by competing with Ch in neuronal and extraneuronal transport mechanisms and in enzyme catalyzed reactions of Ch, reacting irreversibly with the carrier and/or enzyme to interfere with cholinergic mechanisms at synaptic sites and possibly with other metabolic processes involving Ch. (Journal abstract modified)

238830 Demetrescu, M. University of California, Irvine, CA 92717 **Cortical disinhibition: a possible mechanism for drug-induced hallucinations.** Federation Proceedings. 35(3):768, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a possible mechanism for drug induced hallucinations was reported in cats. In cats with rostral pontine brainstem transections, the recovery cycle of cellular groups in the visual cortex was automatically sampled by progressively increasing the pairing interval (PI) of 256 successive pairs of stimuli delivered to the lateral geniculate body (LGB) from 5 to 240 msec. Cell spikes in response to second stimulus of each pair were displayed in a three dimensional reference system with amplitude shown on the horizontal, and PI shown on the depth axis. Inhibition of firing starting at 10-20 and ending at 60-100 msec PIs is typical throughout the visual cortex. A dramatic postanesthetic rebound, with cells firing in the area where previously they were totally inhibited (20-60 msec PI), lasted up to 3 hrs. It is suggested that the background of cortical disinhibition is common to, and may be responsible for, both dreaming and hallucinations known to occur in human subjects, respectively, during sleep and during ketamine postanesthesia. (Journal abstract modified)

238836 Messiha, F. S. Department of Pharmacology, Texas Tech University School of Medicine, Lubbock, TX 79409 **Evaluation of cesium chloride as antidepressant.** Federation Proceedings. 35(3):784, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, an evaluation of cesium chloride (CsCl) as an antidepressant was reported. Semichronic administration of rubidium chloride (RbCl) or CsCl significantly decreased the duration of ethanol (ETOH) produced narcosis in mice. In motility tests, administration of CsCl for 5 days significantly reduced chlorpromazine and L-dopa produced behavioral depression in mice. Administration of CsCl or RbCl at 3.0mEq/kg i.p. reduced voluntary alcohol consumption in the rat. The results suggest a different order of mobility in these ions across cell membrane, show antidepressant properties for Cs+, and indicate its potential in negating some of ETOH mediated effects. (Journal abstract modified)

238837 Mitchell, C. L; Conway, A. C.; Tresnak, N. J.; Hammar, W. J. Riker Labs, Inc., 3M Co., St. Paul, MN 55101 **Pharmacology of R-806, a tetracyclic antidepressant.** Federation Proceedings. 35(3):784, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the pharmacology of 10,11-dihydro-12-anti-dimethylaminomethyl-5,10-methano-5H dibenzo (a,d) cycloheptane hydrochloride (R-806) was reported. It was noted that R-806: has an antidepressant profile similar to imipramine but with less depressant and anticholinergic activities; is efficacious in antagonizing the effects of both reserpine and Ro4-1284; produces mortality in mice receiving sublethal doses of l-epinephrine or L-dopa; in contrast to imipramine, produces an increase in locomotor activity in mice and avoidance responding in the Sidman avoidance test in both rats and monkeys; like the tricyclic compounds, potentiates the pressor responses to exogenously administered catecholamines in dogs. Unlike imipramine, the depressor responses evoked by acetylcholine or peripheral vagal stimulation are not altered by R-806. In the isolated guinea-pig ileum, R-806 is approximately 0.005 as active as chlorpheniramine against histamine, 0.0005 as active as atropine against acetylcholine and 0.1as active as phentolamine against serotonin. (Journal abstract modified)

238838 Lewis, D. E.; Isaac, L. Department of Pharmacology, University of Illinois Medical Center, Chicago, IL 60680 **Effects of antihistaminic drugs on feline brain monoamine metabolism.** Federation Proceedings. 35(3):784, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of antihistaminic drugs on feline brain monoamine metabolism were reported. Diphenhydramine (DPA) and phenindamine (PDM) were administered in various doses to cats, and the time course of changes in amine metabolite levels in cerebrospinal fluid (CSF) were determined. DPA at a sedative dose did not alter 5-hydroxytryptamine (5HT) or dopamine metabolism. Excitant doses of DPA elevated 5-hydroxyindolacetic acid (5HIAA) levels while homovanillic acid (HVA) levels remained unchanged. At a convulsant dose, it lowered rectal temperature while elevating both 5HIAA and HVA levels. PDM reportedly produces only central nervous system (CNS) excitation and convulsions. It caused stereotypy and excitation while elevating both 5HIAA and HVA levels in CSF. These data suggest that antihistaminic induced drowsiness is not due to an alteration in brain 5HT or dopamine metabolism and that only 5HT metabolism is increased during CNS excitation. Finally, stereotypic behavior following PDM may occur through a dopaminergic system as reflected by the elevated levels of HVA in CSF. (Journal abstract modified)

238839 Geyer, Harry M.; Ridlon, Seward A.; Schacht, Ulrich; Novick, William J., Jr. Hoechst-Roussel Pharmaceuticals Inc., Somerville, NJ 08876 **Pharmacological studies with HP 505, a potential antidepressant compound.** Federation Proceedings. 35(3):784, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the antidepressant activity of HP-505 (1,3 dihydro-3-phenylspiro(isobenzofuran-1,4'-piperidine)) was reported. In preventing ptosis produced by tetrabenazine, HP-505 was found to be more potent than desipramine (DMI) with an oral ED50 of 1.4mg/kg compared to 2.3mg/kg for DMI. HP-505 also prevents reserpine induced hypothermia in mice and is an inhibitor of rat muricidal activity. The ability of HP-505 to inhibit neuronal uptake of biogenic amines was elucidated using the rat brain synaptosomal preparation. HP-505 was found to block C14-norepinephrine uptake in whole brain and in the hypothalamus, being superior to DMI. Additionally, HP-505 was unique in preventing the uptake of H3-dopamine in the striatum. On inhibiting C14-serotonin uptake HP-505 was more active than DMI and compared favorably to chlorimipramine. HP-505 was also found to increase spontaneous motor activity in mice, and to produce an EEG alerting response in cats without overt hyperactivity. The pharmacological profile suggests that HP-505 is an activating rather than a sedative type of antidepressant. (Journal abstract modified)

238840 Bymaster, Frank P.; Wong, David T. Lilly Research Laboratories, Indianapolis, IN 46206 **Nisoxetine (Lilly 94939) selectively blocks the uptake of norepinephrine in vitro and in vivo in rat brain.** Federation Proceedings. 35(3):784, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of nisoxetine

(Lilly 94939) (N) on the uptake of norepinephrine (NE) in vitro and in vivo in the rat were reported. It was noted that N inhibits the uptake of NE by synaptosomes of hypothalamus, brainstem, and cerebral cortex of rat brain with inhibitor constants (Ki values) of 1, 2, and 6nM, respectively. In corpus striatum, however, the Ki value for N to inhibit the uptake of dopamine (DA) is 360 nM. Thus, N has about 200 fold greater affinity for the uptake sites of NE than for those of DA. N administered at 10mg/kg i.p. to rats reduced the uptake of catecholamines by synaptosomes of brain regions with hypothalamus being inhibited 70%, brainstem and cerebral cortex about 55%, and striatum 25%. N decreased the uptake of NE in cerebral cortical synaptosomes isolated from the N treated rats in a dose dependent fashion with an ED50 of 7.5mg/kg i.p. The data suggest that N is a potent and selective inhibitor of NE uptake by nerve terminals of various rat brain regions. (Journal abstract modified)

238841 Borison, R. L.; Maslanka, A. Chicago Medical School, Chicago, IL 60612 **2-Phenylethylamine (PEA) in d-amphetamine induced extrapyramidal disorders.** Federation Proceedings. 35(3):784, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effect of 2-phenylethylamine (PEA) in d-amphetamine (D-AMPH) induced extrapyramidal disorders were reported in guinea pigs. In male albino guinea pigs, chronic intraperitoneal injection of D-AMPH, 7mg/kg/day induced hyperactivity, gnawing and other sterotypias with reverse tolerance to the intensity and latency of these effects. Chronic PEA alone or with a monoamine oxidase inhibitor, pargyline, as well as D,L-dihydroxyphenylalanine (DOPA) induces similar sterotypias, but in neither case was sensitization observed. In animals pretreated with chronic D-AMPH, changing to chronic PEA plus pargyline maintained pattern and latency of sterotyped behavior, whereas changing to DOPA did not maintain sterotypias and activity was reduced. These results, plus the ability of PEA to reverse drug-induced parkinsonism in animals and the reduced excretion of PEA in parkinsonian parients suggests that PEA may play a role in extrapyramidal dopaminergic synapses. (Journal abstract modified)

238846 Abdallah, A. H.; Riley, C. C.; Roby, D. M.; Boeckler, W. Dow Chemical Company, Midland, MI 48640 **The effect of DL-254 on the pharmacological activities of d-amphetamine and apomorphine: a comparison with antianxiety and neuroleptic agents.** Federation Proceedings. 35(3):785, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effect of DL-254 (1-(2-hydroxyethyl)-2-thio-3-(2,4-xylyl)-urea) on the pharmacological activities of d-amphetamine (AM) and apomorphine (APO) were reported in rodents. The administration of either DL-254 or diazepam (DIAZ) did not significantly antagonize the hyperthermic effect of AM. However, chlorpromazine (CPZ) and haloperidol (HAL) were highly effective. CPL and HAL were effective in protecting against AM aggregation lethality; DL-254 and DIAZ were ineffective. HAL and CPZ caused significant reduction of the stimulant effect of AM, whereas DL-254 and DIAZ were ineffective. CPZ and HAL were very effective in blocking APO induced rearing in mice. Their ED50s were 1.9and 0.3mg/kg, respectively. However, DL-254 and DIAZ had weak effects. It is concluded that DL-254 is similar to DIAZ in that it lacks the ability to antagonize the effects of AM and APO in mice, whereas CPZ and HAL showed substantial antagonism. (Journal abstract modified)

238849 Truitt, Edward B., Jr.; Vaughen, Christina M. George Washington University School of Medicine, Washington, DC 20037 **Effects of lithium on chronic ethanol consumption and behavior.** Federation Proceedings. 35(3):814, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of lithium on chronic ethanol consumption and behavior were reported in rats. Male, Sprague-Dawley and Wistar strain rats were given a nutritionally complete liquid diet containing ethanol as the sole source of liquids and calories. Lithium chloride was given in the diet or intraperitoneally for short periods. Behavior was measured by rotorod performance and semiquantitative observational scores for arousal, nociceptive reflex, startle reaction and ataxia. Lithium chloride reduced alcohol diet consumption and improved rotorod performance but the effect was not sustained. It was effective by both routes of administration which discounts a mechanism of taste aversion. These results were interpreted using a biogenic amine hypothesis for the central effects of ethanol. (Journal abstract modified)

238971 Yamamoto, Ken-ichi. Division of Neuropharmacology, Shionogi Research Laboratory, Fukushima-Ku, Osaka 553, Japan **Neurohumoral mechanisms relating to circadian sleep-wakefulness cycles of humoral experimental animals.** Advances in Neurological Sciences (Tokyo). 19(4):771-778, 1975.

Electroencephalography (EEG), biochemical and behavioral studies were carried out in six species of animals with chronically implanted brain electrodes for neuropharmacological analysis of circadian sleep-wakefulness cycles. Results indicate differences in the normal EEG pattern and sleep-wakefulness cycles among animal species as well as differences in the circadian rhythm or neurohormones in animal brain according to species. Differences in route of drug administration sometimes caused differences in alteration of the sleep-wakefulness cycle. Differences in site of action of drugs frequently caused different alterations of sleep cycles. 56 references. (Author abstract modified)

239044 Osnes, Jan-Bjorn; Christoffersen, Thoralf; Morland, Jorg; Oye, Ivar. Institute of Pharmacology, University of Oslo, P.O. Box 1057, Blindern, Oslo, Norway **Chlorpromazine and hormonal elevation of cyclic AMP contents in turkey erythrocytes and perfused rat heart and liver.** Acta Pharmacologica et Toxicologica (Kobenhavn). 38(3):195-208, 1976.

An investigation was carried out to determine whether chlorpromazine (CPZ) affected the elevation of cyclic adenosine monophosphate (AMP) by isoprenaline in turkey erythrocytes and perfused rat hearts, and by glucagon in perfused rat liver. In the perfused heart the incorporation of 14C-adenine (in the perfusate) into the cyclic AMP pool, was also measured. In turkey erythrocytes exposed to isoprenaline the cyclic AMP accumulation was markedly inhibited by CPZ at concentrations above .05mM whereas lower concentrations caused slight reduction of cyclic AMP elevation. In the perfused rat heart and liver CPZ, at concentrations compatible with the integrity of the organ, did not reduce or change the cyclic AMP increase after isoprenaline and glucagon, respectively. The results indicate that inhibition of adenylate cyclase activation is not a general feature of the membrane stabilizing effects of CPZ. The loss of cyclic AMP response in turkey erythrocytes exposed to high concentrations of CPZ may be related to impairment of the cell membrane. CPZ could not be used as a tool in an attempt to discriminate between cyclic AMP mediated and cyclic AMP independent hormone effects. 27 references. (Author abstract modified)

239085 Palmer, G. C. Dept. of Pharmacology, School of Medicine, Univ. of New Mexico, 915 Stanford, N.E., Albuquerque, NM 87131 **Influence of tricyclic antidepressants on the adenylate cyclase-phosphodiesterase system in the rat cortex.** Neuropharmacology (Oxford). 15(1):1-7, 1976.

The actions of 10 tricyclic antidepressant drugs were evaluated with respect to inhibition of the adenylate cyclase/cyclic adenosine 3':5'-monophosphate (cyclic-AMP) phosphodiesterase system in various preparations of rat cerebral cortex. At highest concentrations all drugs exhibited antagonism of the stimulation of cyclic-AMP accumulation by norepinephrine in incubated tissue slice (whole cell) preparations. In these experiments iprindole and desipramine were the most potent agents, while lesser degrees of inhibition were seen with amitriptyline, chlorimipramine, nortriptyline, protriptyline, imipramine, opipramol, 2-hydroxyimipramine and 2-hydroxydesipramine in approximately that order. On the other hand, in broken cellular preparations from isolated neuronal and glial enriched fractions, extremely high concentrations of the tricyclic antidepressants were necessary to inhibit by 50% the basal, fluoride sensitive (catalytic site) and norepinephrine sensitive (receptor) components of adenylate cyclase. In similar studies with isolated neuronal and glial fractions somewhat lower concentrations of tricyclic antidepressants were required to inhibit by 50% the total phosphodiesterase activity. The data indicate that results obtained from intact cellular investigations may not always be extrapolated to similar findings with enzyme preparations derived from broken cells. 37 references. (Author abstract)

239086 Shih, T.-M.; Khachaturian, Z. S.; Barry, H., III; Hanin, I. Dept. of Psychiatry, Western Psychiatric Institute and Clinic, School of Medicine, Univ. of Pittsburgh, Pittsburgh, PA 15261 **Cholinergic mediation of the inhibitory effect of methylphenidate on neuronal activity in the reticular formation.** Neuropharmacology (Oxford). 15(1):55-60, 1976.

Cholinergic mediation of the inhibitory effect of methylphenidate on neuronal activity in the reticular formation was studied in rats. Methylphenidate hydrochloride markedly attenuated the discharge rates of neurons in the mesencephalic reticular formation of immobilized rats. This effect of methylphenidate was mimicked by oxotremorine and nicotine, unaffected by atropine, and abolished by mecamylamine. A central action of oxotremorine and nicotine was indicated by the further finding that atropine, but not methyl atropine, blocked the effect of oxotremorine, and that mecamylamine but not hexamethonium blocked the effect of nicotine. These results suggest that cholinergic mechanisms might mediate the electrophysiological effect of methylphenidate in the mesencephalic reticular formation and also the therapeutic effect of this drug in hyperactive children. 51 references. (Author abstract)

239087 Waller, M. B.; Myers, R. D.; Martin, G. E. Lab. of Neuropsychology, Purdue Univ., Lafayette, IN 47907 **Thermoregulatory deficits in the monkey produced by 5,6-dihydroxytryptamine injected into the hypothalamus.** Neuropharmacology (Oxford). 15(1):61-68, 1976.

5,6-Dihydroxytryptamine (5,6-DHT), an agent which destroys serotonergic nerve endings, and serotonin were injected in rhesus monkeys on different days and thermoregulatory effects were measured. The initial effect of 5,6-DHT was dose dependent hyperthermia similar to that evoked earlier by serotonin. Severe thermoregulatory deficits in response to the cold challenge were observed on subsequent days after low doses of 5,6-DHT were injected primarily in the region of the anterior hypothalamus. Impairment in thermoregulation to the warm temperature also occurred after higher doses of the neurotoxin were given. However, serotonin still evoked a temperature response nearly identical to that seen before 5,6-DHT treatment. These results support the theory that serotonergic neurons in the hypothalamus are involved in the central control of body temperature in the primate. 27 references. (Author abstract modified)

239090 Myllyla, V. V. Dept. of Neurology, University Central Hospital of Oulu, SF-90220 Oulu 22, Finland **Effect of convulsions and anticonvulsive drugs on cerebrospinal fluid cyclic AMP in rabbits.** European Neurology (Basel). 14(2):97-107, 1976.

Cyclic adenosine 3',5'-monophosphate (cAMP) concentration and aspartate amino transferase (ASAT or GOT) activity were measured from cerebrospinal fluid (CSF) of rabbits before and after electrically induced convulsions. The convulsions caused a significant increase in CSF cAMP concentration. Treatment with phenobarbital, diphenylhydantoin and carbamazepine for 7 days decreased the basal cAMP values in CSF and partly inhibited the rise after the convulsions. The alterations in ASAT activity were parallel but less striking. The results suggest the involvement of cAMP in epileptic discharge and in the mechanism of action of anticonvulsants. 38 references. (Author abstract)

239261 Acosta-Urquidi, Juan; Chase, Ronald. Dept. of Zoology, University of Toronto, Toronto, Ontario M5S 1A8, Canada **The effects of delta9-tetrahydrocannabinol on action potentials in the mollusc Aplysia.** Canadian Journal of Physiology and Pharmacology (Ottawa). 53(5):793-798, 1975.

The effects of delta9-tetrahydrocannabinol (delta9-THC) on action potentials were examined during intrasomatic recordings from the isolated buccal and parietovisceral ganglia of Aplysia californica. When added to the saline solution bathing the preparation, the compound caused a reduction in spike overshoot and increased the lability of responses to electrical stimulation. The somatic membrane appeared to be more affected than the axonal membrane. It is suggested that diffusion barriers in the ganglion probably account for the high degree of variability in drug response, such that both of the characteristic changes were observed in only about 30% of the tests. The results indicate that delta9-THC causes a depression in nerve cell excitability, and these data are consistent with reported effects of THC compounds in mammals. 15 references. (Author abstract modified)

239307 Koslow, Stephen H. Clinical Research Branch, NIMH 5600 Fishers Lane; Rockville, MD 20853 **The biochemical and biobehavioral profile of 5-methoxytryptamine. (Unpublished paper).** Rockville, MD, NIMH, 1976. 35 p.

A biochemical and biobehavioral profile of 5-methoxytryptamine (5-MT), an indolealkylamine resembling serotonin, is presented. A review of the literature supports the view that 5-MT may have a functional role in the mammalian central nervous system. Additional research is recommended to clarify the biological role of 5-MT. It is known to be found in neural tissues and to be capable of altering animal behavior and modifying some chemical constituents of the brain. It is concluded that, although 5-MT is only present in trace concentrations, it is a potentially significant biological compound. 4 references. (Author abstract modified)

239577 Mrsulja, Bogomir B.; Mrsulja, Branislava J.; Spatz, Maria; Klatzo, Igor. Lab. of Neuropathology and Neu-

roanatomical Sciences, NINCDS, NIH, Bethesda, MD 20014 **Catecholamines in brain ischemia -- effects of alpha-methyl-p-tyrosine and pargyline.** Brain Research (Amsterdam). 104(2):373-378, 1976.

The effects of alpha-methyl-p-tyrosine (AMPT) and pargyline on catecholamine levels of ischemic brains of Mongolian gerbils were determined. The reduction of both dopamine (DA) and norepinephrine (NE) in cerebral ischemia of gerbils is reported. Additional catecholamine reduction was observed in animals treated with AMPT prior to the ischemic exposure; lower accumulation of DA and NE was obtained in ischemic animals pretreated with pargyline. Relative uptake of (3H)NE was decreased about 55% but relative release was increased about 62% in synaptosome preparation obtained from the ischemic brain. Results support the contention of increased catecholamine release occurring in ischemia. 22 references.

239581 Diez, James A.; Sze, Paul Y.; Ginsburg, Benson E. Dept. of Biochemistry and Nutrition, School of Medicine, Univ. of North Carolina, Chapel Hill, NC 27514 **Tryptophan regulation of brain tryptophan hydroxylase.** Brain Research (Amsterdam). 104(2):396-400, 1976.

The effects of alterations in brain tryptophan levels, achieved by injection of the amino acid or glucocorticoid, on the level of tryptophan hydroxylase activity were examined in the mouse. Hydrocortisone acetate (HCA) and tryptophan were administered i.p.,mice were subsequently sacrificed and tryptophan hydroxylase, tryptophan, and protein were assayed from brain homogenates. A single injection of HCA produced an elevation of brain tryptophan levels which was both rapid and prolonged. Brain tryptophan levels in mice receiving tryptophan injections were not elevated at the time of sacrifice. There was a 26% increase in tryptophan hydroxylase activity in the group receiving multiple tryptophan injections; this was significantly greater than the activity in both the controls and the group receiving HCA. Combined administration of HCA and tryptophan resulted in a 19% increase in tryptophan hydroxylase activity. It is concluded that results are consistent with an action of tryptophan which would either stabilize tryptophan hydroxylase against degradation or actually induce its synthesis. 19 references.

239582 Spiker, Maura D.; Palmer, Gene C.; Manian, Albert A. Dept. of Pharmacology, Univ. of New Mexico School of Medicine, Albuquerque, NM 87131 **Action of neuroleptic agents on histamine-sensitive adenylate cyclase in rabbit cerebral cortex.** Brain Research (Amsterdam). 104(2):401-406, 1976.

The structure/activity relationship of neuroleptic actions and histamine sensitive adenylate cyclases was investigated in rabbit cerebral cortex. Tissue slices from the cerebral cortex were prepared and incubated, determination of cyclic adenosine monophosphae (AMP) was carried out, and data from all samples containing neuroleptic agents were compared to either respective control or histamine stimulated levels of cyclic AMP from the same animal. Neuroleptic agents were also added to the adenylate cyclase enzyme prepared from isolated neuronal and glial enriched fractions, and the concentrations of each drug needed to give 50% inhibition of adenylate cyclase are reported. 20 references.

239661 Misra, Radhey S.; Barthwal, Jayanti P.; Parmar, Surendra S.; Singh, Shiva P.; Stenberg, Virgil I. Bio-Organic Laboratory, Michigan Cancer Foundation, Meyer L. Prentis Cancer Center, Detroit, MI 48201 **Synthesis of substituted thiobenzoxazoles/benzothiazoles: inhibition of cellular respiratory and monoamine oxidase activities and anticonvulsant property.** Journal of Pharmaceutical Sciences. 65(3):405-408, 1976.

Several 2-(substituted alkoxy/hydrazinocarbonyl acetanilidothio) benzoxazoles/benzothiazoles were synthesized and characterized by their sharp melting points, elemental analyses, and infrared spectra. All thiobenzoxazoles/benzothiazoles possessed low anticonvulsant activity, which was reflected by the 10-40% protection afforded by these compounds against pentylenetetrazol induced convulsions. All thiobenzoxazoles/benzothiazoles inhibited selectively the nicotinamide adenine dinucleotide (NAD) dependent oxidation of pyruvate, DL-isocitrate, and alpha-ketoglutarate by rat brain homogenates. NAD independent oxidation of succinate remained unaltered. All 2-(substituted hydrazinocarbonyl acetanilidothio)benzoxazoles/benzothiazoles inhibited monoamine oxidase activity of rat brain homogenates. Greater monamine oxidase inhibition was observed with thiobenzothiazoles than with the corresponding thiobenzoxazoles. The low anticonvulsant activity possessed by these thiobenzoxazoles/benzothiazoles was found to be unrelated with their ability to inhibit cellular respiratory and monoamine oxidase activities of rat brain homogenates. 12 references. (Author abstract)

239662 Singh, Shiva P.; Ali, Basheer; Auyong, Theodore K.; Parmar, Surendra S.; De Boer, Benjamin. Dept. of Chemistry, University of North Dakota, Grand Forks, ND 58202 **Anticonvulsant activity and selective inhibition of nicotinamide adenine dinucleotide-dependent oxidations by 10-(2-arylimino-3-acetylamino-4-thiazolidonyl) phenothiazines.** Journal of Pharmaceutical Sciences. 65(3):391-396, 1976.

Several 10(1-acetyl-4-arlthiosemicarbazido)phenothiazines and their corresponding cyclized 10-(2-arylimino-3-acetylamino-4-thiazolidonyl) phenothiazines were synthesized and characterized by their sharp melting points and elemental analyses. All compounds inhibited nicotinamide adenine dinucleotide (NAD) dependent oxidation of pyruvate and alpha-ketoglutarate selectively, whereas NAD independent oxidation of succinate remained unaltered. All phenothiazine derivatives exhibited anticonvulsant activity, which was reflected by the 20 - 60% protection observed against pentylenetetrazol induced convulsions in mice. The ability of substituted thiosemicarbazidophenothiazines to inhibit cellular respiratory activity was reduced considerably by cyclization to the corresponding substituted thiazolidinophenothiazines. On the other hand, cyclization generally resulted in increased anticonvulsant activity. Thus the anticonvulsant activity possessed by these substituted phenothiazines bore no relationship with their ability to inhibit selectively the NAD dependent oxidations. 14 references. (Author abstract modified)

239685 Amico, D. J. D.; Calne, D. B.; Klawans, Harold L. Abraham Lincoln School of Medicine, Univ. of Illinois, Chicago, IL **Altered hypothermic responsiveness to (+)-amphetamine.** Journal of Pharmacy and Pharmacology (London). 28(2):154-156, 1976.

Hypothermic response is reported to (+)-amphetamine sulfate or apomophine hydrochloride in guinea pigs at 4 degrees, in agreement with previous observations in the rat. A dopaminergic mechanism is implicated by the ability of apomorphine, a compound which is thought to act directly on dopamine receptors to elicit hypothermia; and by the ability of pimozide, a blocker of dopamine receptors, to eliminate the hypothermic response. However, the data presented concerning acute chlorpromazine pretreatment are difficult to interpret with regard to antidopaminergic properties alone; possibly the drug interacts with a number of thermoregulatory systems. The study supports the role of dopamine in thermoregulation,

and indicates that such mechanisms are susceptible to pharmacological alteration. Results show that chronic pretreatment schedules which induced hypersensitivity to one dopaminergic response can produce tolerance to another response. 10 references.

239787 Klee, W. A. Laboratory of General and Comparative Chemistry, NIMH, Bethesda, MD 20014 **Opiate receptors in cell cultures. (Unpublished paper).** Bethesda, MD, NIMH, 1976. 1 p.

A neuroblastoma x glioma hybrid cell line (NG108-15) has been found to contain 300,000 opiate receptors/cell. The parental lines and other neuroblastoma and hybrid lines examined have few or no opiate receptors. Adenylate cyclase activity in NG108-15 is strongly inhibited by morphine and other opiates. Such inhibition is found only in cells containing opiate receptors, is reversed by opiate antagonists, and inhibitory activity of a series of drugs correlates well with affinity for receptors. Thus, these receptors are functionally linked to adenylate cyclase in this cultured cell system. Similar data have been obtained in rat brain homogenates. Long-term exposure of NG108-15 to opiates produces a compensatory increase in adenylate cyclase activity. This late positive regulation can account for the tolerance and dependence phenomena of opiate addiction. Endogenous peptides with morphine like activity also inhibit adenylate cyclase through morphine receptors in this cell line. 3 references. (Author abstract modified)

239828 Fenske, M.; Wuttke, W. Max-Planck-Institute for Biophysical Chemistry, Dept. of Neurobiology, 3400 Gottingen-Nikolausberg, Germany **Effects of intraventricular 6-hydroxydopamine injections on serum prolactin and LH levels: absence of stress-induced pituitary prolactin release.** Brain Research (Amsterdam). 104(1):63-70, 1976.

Effects of intraventricular 6-hydroxydopamine (6-OHDA) injections on serum prolactin and luteinizing hormone (LH) levels were explored. Serum prolactin levels in male rats injected with 6-OHDA were significantly higher than in untreated control rats. Intraventricular injection of male rats with artificial cerebrospinal fluid resulted in elevated mean prolactin levels similar to those observed in 6-OHDA treated animals. Prolactin levels in 6-OHDA treated rats are continuously elevated, whereas they rise from basal levels to extremely high levels in cerebrospinal fluid (CSF) treated rats, thus resulting in similar mean values. The CSF treated controls are hypersensitive to the stress of being removed from their normal environment. Such an effect was not observed in 6-OHDA treated nor in untreated, and thus stress inexperienced, rats. Serum prolactin and LH levels were followed over a period of 71 days after 6-OHDA treatment. Prolactin levels increased within 1 day after treatment and stayed at a high level of 15 days. Subnormal prolactin values were measured 37 days after 6-OHDA treatment. Serum LH levels were below normal 3 h and 1 day and were increased 37 and 71 days after 6-OHDA treatment. 26 references. (Author abstract modified)

239832 Klara, Peter M.; Kostrezewa, Richard M.; Brizzee, Kenneth R. Dept. of Anatomy and Pharmacology, Tulane University, New Orleans, LA 70112 **Destructive action of systemically administered 6-hydroxydopamine on the rat area postrema.** Brain Research (Amsterdam). 104(1):187-192, 1976.

A study undertaken to determine whether 6-hydroxydopamine (6-OHDA) is able to exert its toxic effect on the rat area postrema (AP) when administered systemically in high doses is reported. Eight rats received 6-OHDA while four control rats received only saline. Degeneration of neuronal processes within the perivascular spaces and outside the basal lamina within the AP parenchyma were observed at 2 and 24 hours after 6-OHDA. These effects did not change significantly between 2 and 24 hours. While degeneration products were observed in neuronal elements, glia and ependyma showed evidence of lysosomal induction of phagocytic activity. 24 references.

239836 Gahwiler, B. H. Sandoz Ltd., Biological and Medical Research Division, CH-4002 Basel, Switzerland **Inhibitory action of noradrenaline and cyclic AMP in explants of rat cerebellum.** Nature (London). 259(5543):483-484, 1976.

The hypothesis that cyclic adenosine-3′,5′-monophosphate (cAMP) mediates the depressant action of norepinephrine (NE) on Purkinje cells was investigated in cultured Purkinje cells from rat cerebellum. Results indicate that high concentrations of cAMP only slightly decrease the firing rate of Purkinje cells, but low concentrations of phosphodiesterase inhibitors strongly enhance the inhibition induced by cAMP and NE. Papaverine was about 100 times more potent than aminophylline and caffeine in this respect. The facts that NE and phosphodiesterase inhibitors produce similar electrophysiological results and that the enzyme inhibitors enhance the action of NE strengthen the hypothesis that cAMP serves as a second messenger for NE in the cerebellum. The weak effect of cAMP on Purkinje cell firing is attributed to the high level of phosphodiesterase activity in the cerebellum. 14 references.

239849 Leonard, B. E. Dept. of Pharmacology, University College, Galway, Ireland **Acute and chronic effects of 4-chloroamphetamine on monoamine metabolism in the rat brain.** Psychopharmacologia (Berlin). 46(1):11-18, 1976.

The effects of 4-chloramphetamine (4-CA) on serotonin and catecholamine metabolism in the rat brain were compared. The acute administration of 4CA caused a marked reductin in the concentration of serotonin and 5-hydroxyindoleacetic acid and a rise in dopamine in the rat brain. Following the injection of 3H/tyrosine and 3H tryptophane into rats treated with 4-CA there was a reduction in brain levels of 3H dopamine and 3H serotonin. Although the endogenous concentration of noradrenaline was not affected by 4-CA, there is evidence that its reuptake into neurones was reduced and its release increased by the drug. Following the administration of 4-CA for 10 days, the concentration of 5-hydroxyindoleacetic acid was reduced; no other changes in amine metabolism were apparent. It appears that following acute administration, 4-CA has a neurochemical profile which is similar to that of many tricyclic antidepressants. However, there is a marked discrepancy between the acute and chronic effects of 4-CA on brain amine metabolism. Such findings are difficult to reconcile with the widely accepted theory that antidepressant drugs counteract the symptoms of depression by increasing the concentration of noradrenaline and/or serotonin at receptor sites within the brain. 39 references. (Author abstract)

239851 De Wied, D.; Gispen, W. H. Rudolf Magnus Inst. for Pharmacology, Univ. of Utrecht, Utrecht, The Netherlands **Impaired development of tolerance to morphine analgesia in rats with hereditary diabetes insipidus.** Psychpharmacologia (Berlin). 46(1):27-29, 1976.

The development of tolerance to daily administration of morphine-HCl (10mg/kg i.p.)was studied in a series of trials on a hot plate using rats with hereditary diabetes insipidus (DI), which lack the ability to synthesize vasopressin. In contrast to heterozygous DI rats, who developed full tolerance after the fifth injection, homozygous (HO) DI rats showed a delayed

development of tolerance. Substitution of HO-DI rats with either argininet8-vasopressin (3 micrograms/rat, s.c. daily) or the endocrinologically inert fragment of vasopressin desglycinamide lysine-8-vasopressin (5 micrograms/100 g, s.c. daily) restored the impaired development of tolerance towards normal. The data support the notion that vasopressin is important to the development of tolerance to narcotic analgesics and that its mechanisms of action is dissociated from its endocrine effect but rather resembles that of its known influence on memory consolidation. 13 references. (Author abstract modified)

239854 Blasig, J.; Hollt, V.; Herz, A.; Paschelke, G. Max-Planck-Institut fur Psychiatrie, Abt. Neuropharmakologie, D-8000 Munich 40, Kraepelinstrasse 2, Germany **Comparison of withdrawal precipitating properties of various morphine antagonists and partial agonists in relation to their stereospecific binding to brain homogenates.** Psychopharmacologia (Berlin), 46(1):41-51, 1976.

In morphine dependent rats the withdrawal preciptating properties of various morphine antagonists and partial agonists were studied by quantitatively evaluating a variety of different withdrawal signs. A comparison of the dose response curves of the various substances obtained for the different signs revealed marked differences in respect to the lowest effective doses (EDs) necessary to precipitate the withdrawal signs as well as in the maximum frequencies of the signs induced. The pure antagonist, naloxone, which was judged very potent according to the ED, precipitated the lowest levels of jumping, whereas certain partial agonists of the benzomorphane type, which were less potent according to the ED, induced very high levels of this sign. These latter compounds, however, failed to precipitate complete withdrawal, as evidenced by the absence of some of the withdrawal signs. The jumping precipitating potency of the antagonists as judged from the ED was found to be highly correlated to the stereospecific binding of these substances to rat brain homogenate. However, the ability of the substances of precipitate high levels of jumping was seen to increase with increasing degree of agonistic properties, as indicated by the ratio of stereospecific binding in the presence and absence of sodium. 32 references. (Author abstract modified)

239855 Korr, H.; Seiler, N. Institut fur Strahlenkunde der Universitat Wurzburg, D-8700 Wurzburg, Versbacher Ladstr. 5, Germany **Autoradiographic studies on the distribution of 3H-2,3,4-trimethoxy-beta-phenylethylamine in the mouse.** Psychopharmacologia (Berlin). 46(1):53-58, 1976.

The regional distribution of radioactivity was studied in the brain and other organs of the mouse by light microscopic autoradiography after injection of 3H-2,3,4-trimethoxy-beta-phenylethylamine(2,3,4-TMPEA), a nonhallucinogenic isomer of mescaline. The distribution patterns were compared with biochemical and autoradiographic results obtained after 3H-mescaline. Although 2,3,4-TMPEA is rapidly deaminated compared to mescaline, its distribution pattern in the brain is similar to that of mescaline at 1 h after injection. However, contrary to mescaline, the radioactive labeling becomes more and more homogenously distributed in the brain with time. The distribution patterns in kidney, pancreas, adrenal, and spinal ganglia were also different from those observed after application of 3H-mescaline. 25 references. (Author abstract)

239858 Bigler, Erin D.; Fleming, Donovan E. Div. of Neurobiology, Barrow Neurological Inst. of St. Joseph's Hospital an Medical Ctr., 330 West Thomas Rd., Phoenix, AZ 86013 **Pharmacological suppression of photically evoked afterdischarges in rats: incremental dose, hippocampal EEG and behavioral activity correlates.** Psychopharmacologia (Berlin). 46(1):73-82, 1976.

In Ss lightly restrained pharmacological arousal via pilocarpine, physostigmine, or amphetamine administration, as compared to saline and methyl atropine treated controls, suppressed photically evoked afterdischarge (PhAD) activity in visual cortex, while concomitantly inducing rhythmical slow wave activity (RSA) in dorsal hippocampus. Incremental doses of amphetamine and pilocarpine correspondingly suppressed PhAD parameters in a dose response fashion. While physostigmine treatment resulted in significant PhAD suppression, this effect could not be quantified in a dose response manner. Incrementally increased cholinergic blockade via atropine administration also suppressed PhAD bursting, yet simultaneously induced large amplitude irregular slow wave activity (LIA) in dorsal hippocampus. When tested under identical conditions but in an unrestrained environment PhADs were similarly suppressed with the concomitant induction of hippocampal patterns as specified in Experiment I; however, general ambulatory activity was differentially affected by the drugs. Amphetamine and atropine markedly enhanced, while pilocarpine and physostigmine suppressed, such activity. In both experiments, previously established PhAD movement, PhAD/RSA/LIA, and RSA/LIA movement relationships, occurring as hypothesized in amphetamine, methyl atropine, and saline treated animals, did not remain fully intact during cholinergic alteration. 35 references. (Author abstract)

239859 Welburn, P. J.; Starmer, G. A.; Chesher, G. B.; Jackson, D. M. Dept. of Pharmacology, Univ. of Sydney, N.S.W., Australia **Effect of cannabinoids on the abdominal constriction response in mice: within cannabinoid interactions.** Psychopharmacologia (Berlin). 46(1):83-85, 1976.

The effect of cannabinoids on the abdominal constriction response in mice was studied. After oral administration to mice, delta9-tetrahydrocannabinol (THC) and cannabinol (CBM) caused a dose dependent suppression of the abdominal constriction response to formic acid. Cannabinol was 50 times less active than THC and cannabidiol (CBD) was without effect. The effects of THC and CBN were additive. CBD antagonised the antinociceptive effects of both THC and CBN in a dose dependent manner. 27 references. (Author abstract)

239862 Ruch, Walter; Asper, Helmuth; Burki, Hans R. Research Institute Wander, Sandoz Research Unit, Berne, Switzerland **Effect of clozapine on the metabolism of serotonin in rat brain.** Psychopharmacologia (Berlin). 46(1):103-109, 1976.

The effect of clozapine on the metabolism of serotonin in rat brain was studied. It is noted that clozapine, but not chlorpromazine, haloperidol, thioridazine, or loxapine, increases the concentrations of tryptophan, serotonin, and 5-hydroxyindoleacetic acid in the rat brain. This effect is due to an increased serotonin synthesis as demonstrated by an enhanced accumulation of 3H-serotonin in the brain after i.v. infusion of 3H-tryptophan. Clozapine also elevates the plasma concentration of free tryptophan, and reduces the plasma concentration of total tryptophan. Therefore, clozapine may increase the brain serotonin concentration by enhancing the availability of tryptophan in the brain, thereby promoting serotonin synthesis. Measurement of the rate of disappearance from the brain of 3H-serotonin or of endogenous serotonin after synthesis in the brain after i.v. infusion of 6-fluorotryptophan shows that clozapine has no direct effect on the release and degradation

of serotonin. It is concluded that the effect of clozapine on brain serotonergic systems may be related to its pronounced sedative and sleep inducing properties. 28 references. (Author abstract modified)

239864 Korr, H. Institut fur Med. Strahlenkunde der Universitat Wurzburg, D-8700 Wurzburg Versbacher Landstrasse 5, Germany **Autoradiographic studies on the distribution of 3H-mescaline in the brain of the marmoset, Callitrix jacchus.** Psychopharmacologia (Berlin). 46(1):115-117, 1976.

Autoradiographs of the brain of the marmoset. Callithrix jacchus, show a strong labeling of the hippocampus and the N. amygdalae 18 h after injection of 3H-mescaline. Six adult male marmosets, received i.p. an injection of 8 mg 2,6-3H-mescaline-HCl in 0.5ml distilled water. One, 3, 6, 18, and 48 h after injection one marmoset (at 18 h, 2 aminals) was decapitated. The brain was quickly removed and frozen by means of solid carbon dioxide. Series of transverse sections were prepared in a cryostat at -18 degrees C, freeze dried, and thereafter treated with gaseous formaldehyde. Contact autoradiographs were prepared from these sections and also from inactive control sections. This study shows a similar distribution pattern of radioactivity in the brain of the marmoset to that previously found in the mouse brain. 18 references. (Author abstract modified)

239957 Gallager, Dorothy W.; Aghajanian, G. K. Dept. of Psychiatry, Yale Univ. School of Medicine, New Haven, CT **Inhibition of firing of raphe neurones by tryptophan and 5-hydroxytryptophan: blockade by inhibiting serotonin synthesis with Ro-4-4602.** Neuropharmacology (Oxford). 15(3):149-156, 1976.

Inhibition of firing of raphe neurons by tryptophan and 5-hydroxytryptophan was examined in the rat. Serotonergic neuronal activity was monitored by extracellular recording from identified cells in the midbrain dorsal raphe nucleus. The systemic administration of L-tryptophan, the initial precursor in the biosynthesis of brain serotonin (5-HT) depressed the firing of serotonergic neurons. The systemic administration of L-5-hydroxytryptophan, the immediate precursor of 5-HT, in combination with a low dose of Ro4-4602, also depressed raphe firing. The tryptophan induced depression of raphe activity was prevented by pretreatment of the animal with the L-aromatic amino acid decarboxylase inhibitor Ro4-4602, in a dose sufficient to block the formation of 5-HT in raphe neurons. p-Chlorophenylalanine, another 5-HT synthesis inhibitor, was ineffective in preventing the depression of raphe firing by tryptophan. Raphe neurons were also inhibited by the local (microiontophoretic) administration of L-tryptophan or L-5-hydroxytryptophan. It is concluded that: (1) both 5-HT precursors (tryptophan and 5-hydroxytryptophan) inhibit raphe firing through their enzymatic conversion to 5-HT; and (2) a local increase in 5-HT within the raphe perikarya is sufficient to lead to a decrease in raphe cellular activity. 54 references. (Author abstract modified)

239959 Marsden, C. A.; Curzon, G. Dept. of Neurochemistry, Institute of Neurology, Queen Square, London WC1 3BG, England **Studies on the behavioural effects of tryptophan and p-chlorophenylalanine.** Neuropharmacology (Oxford). 15(3):165-171, 1976.

The behavioral effects on rats of tryptophan and p-chlorophenylalanine were investigated. p-Chlorophenylalanine decreased brain 5-hydroxytryptamine and increased activity in grouped rats during the light period. In a novel environment, however, activity was reduced. L-Tryptophan (150 mg/kg) restored brain 5-hydroxytryptamine to its original concentration and also reversed the effect of p-chlorophenylalanine on activity of grouped animals. L-Tryptophan (100 mg/kg) caused a partial reversal, while 25 mg/kg had no effect. In control rats, L-tryptophan increased the 5-hydroxytryptamine concentration and turnover, but had no effect on activity. Tryptophan led to a significantly greater increase of 5-hydroxytryptamine and a significantly smaller increase of 5-hydroxyindoleacetic acid in p-chlorophenylalanine treated than in control rats. Although the dopamine antagonist, pimozide, (03 and 1 mg/kg) significantly reduced or blocked the hyperactivity produced by (+)-amphetamine, it did not block the effect of p-chlorophenylalanine on activity. Pimozide also did not block the hyperactivity caused by tranylcypromine plus L-tryptophan although it markedly reduced toxicity. A higher dose (2 mg/kg) of pimozide blocked the effect of p-chlorophenylalanine on activity. 31 references. (Author abstract modified)

239960 Green, A. R.; Youdim, M. B. H.; Grahame-Smith, D. G. MRC Unit, Radcliffe Infirmary, Oxford OX2 6HE, England **Quipazine: its effects on rat brain 5-hydroxytryptamine metabolism, monoamine oxidase activity and behaviour.** Neuropharmacology (Oxford). 15(3):173-179, 1976.

The effects of quipazine (2-(1-piperazinyl)quinoline maleate) on rat brain 5-hydroxytryptamine metabolism, monoamine oxidase activity and behavior were investigated. Quipazine administration to rats produced behavioral changes, including hyperactivity, identical to those seen following tranylcypromine and L-tryptophan. When quipazine was given to rats pretreated with p-chlorophenylalanine, the hyperactivity was enhanced. Alpha-methyl-p-tyrosine pretreatment diminished the behavioral responses. Quipazine did not alter the concentration of brain tryptophan but caused a small rise of brain 5-hydroxytryptamine. Oxidation of 5-hydroxytryptamine and dopamine by monamine oxidase (MAO) was partially inhibited during this period. Tryptamine oxidation, however, was unaffected. In vitro studies demonstrated that quipazine inhibited MAO activity reversibly and competitively. Dopamine and 5-hydroxytryptamine oxidation were more readily inhibited than tryptamine and kynuramine, which suggests that quipazine is predominantly a type-A MAO inhibitor. Quipazine induced hyperactivity was enhanced by administration of deprenil, a type-B MAO inhibitor, but not by the type-A MAO inhibitor clorgyline. Quipazine plus deprenil inhibited oxidation of both 5-hydroxytryptamine (a type-A substrate) and phenylethylamine (a type-B substrate). 26 references. (Author abstract modified)

239961 Matthews, W. D.; Connor, J. D. Dept. of Pharmacology, Milton S. Hershey Medical Center, Pennsylvania State Univ. College of Medicine, Hershey, PA 17033 **Effects of diphenylhydantoin and diazepam on hippocampal evoked responses.** Neuropharmacology (Oxford). 15(3):181-186, 1976.

Diphenylhydantoin and diazepam were compared with regard to their effects on responses to single stimuli, and on posttetanic potentiation of evoked potentials within the hippocampus of anesthetized rats. Interhippocampal afferents to pyramidal cells were stimulated electrically, while extracellular field potentials were recorded at successive depths within the contralateral hippocampus. Recording electrodes penetrated perpendicularly from a surface point homotopic to the site of stimulation. The anticonvulsants (40mg/kg diphenylhydantoin, 5mg/kg diazepam), 30 min after intravenous infusion, depressed posttetanic potentiation in the stratum radiatum. At these doses, responses to single stimuli were essentially unaltered. Doses nearer the toxic range (80mg/kg diphenylhydan-

toin, 10mg/kg diazepam) also reduced posttetanic potentiation in the stratum radiatum, but increased (up to 150%) posttetanic potentiation recorded from granule cells in the area dentata. The results indicate that diphenylhydantoin and diazepam have: (1) selective actions on hippocampal posttetanic potentiation which are site and dose dependent; (2) qualitatively similar end effects on posttetanic potentials in two hippocampal subregions; (3) minimal effects on responses to single stimuli at doses which depress or enhance hippocampal posttetanic potentiation. 28 references. (Author abstract)

239962 Deupree, J. D. Dept. of Pharmacology, Univ. of Nebraska Medical Center, Omaha, NE 68105 **Evidence that diphenylhydantoin does not affect adenosine triphosphatases from brain.** Neuropharmacology (Oxford). 15(3):187-195, 1976.

The effects of diphenylhydantoin on brain sodium and potassium dependent adenosine triphosphatase (NaK-ATPase), p-nitrophenylphosphatase and the calcium dependent adenosine triphosphatase (Ca-ATPase) were examined. The results indicate that: (1) diphenylhydantoin did not stimulate the NaK-ATPase of beef brain sodium iodide treated microsomes or rat brain synaptosomes at nonsaturating or saturating levels of sodium and potassium; (2) the apparent stimulation by diphenylhydantoin under high sodium:potassium ratios reported by other workers can be explained by a potassium contamination in the diphenylhydantoin; (3) diphenylhydantoin did not alter the Michaelis constant for ATP for the NaK-ATPase; (4) diphenylhydantoin did not slowly interact with or alter the NaK-ATPase; (5) diphenylhydantoin did not alter the calcium inhibition of the enzyme; and (6) diphenylhydantoin did not alter the p-nitrophenylphosphatase or Ca-ATPase. It is concluded that, based on these considerations, diphenylhydantoin must be exerting its pharmacological effect by altering a membrane constituent other than the NaK-ATPase. 34 references. (Author abstract)

239963 Davison, M. A.; Koss, M. C. Dept. of Pharmacology, Univ. of Oklahoma College of Medicine, Oklahoma City, OK 73190 **The action of chlorpromazine on the electrodermal response in the cat.** Neuropharmacology (Oxford). 15(3):197-201, 1976.

The action of chlorpromazine on the electrodermal response in the cat was investigated. Chlorpromazine (0.02-2.50mg/kg. i.v.)had a dose dependent depressant action on the electrodermal response evoked by either central brainstem or reflex stimulation in chloralose anesthetized cats. Responses elicited by reflex midbrain, and pontine stimulation were significantly reduced at a lower dose of chlorpromazine (0.10mg/kg) than were responses evoked by stimulation of either the hypothalamus or the medulla (0.50mg/kg). Chlorpromazine did not inhibit the postganglionic peripherally evoked response in the doses administered. 22 references. (Author abstract)

239976 Schmidt, D. E. Tennessee Neuropsychiatric Institute, Nashville, TN **Regional levels of choline and acetylcholine in rat brain following head focused microwave sacrifice: effect of (+)-amphetamine and (+or-)-parachloroamphetamine.** Neuropharmacology (Oxford). 15(2):77-84, 1976.

The effect of (+)-amphetamine and (+or-)-p-chloroamphetamine on the levels of choline and acetylcholine (ACh) in discrete regions of rat brain were studied. Animals were sacrificed by head focused microwave irradiation which terminated all measurable enzymatic activity in brain within 2 seconds. Both p-chloroamphetamine and amphetamine induced short-term (less than 48 hr) increases in ACh levels in the striatum and cerebellum and simultaneous decreases in ACh levels in the hippocampus and cortex. In addition, p-chloroamphetamine caused a long-term (greater than 48 hr) increase in ACh levels in the striatum and cerebellum. It is suggesetd that the short-term change in ACh levels induced by p-chloroamphetamine and amphetamine are mediated via release of dopamine, while the long-term changes in ACh levels caused by p-chloroamphetamine are related to serotonin and may indicate that serotonin is involved in the regulation of ACh turnover in the striatum. 56 references. (Author abstract)

239977 Hanbauer, I.; Costa, E. Section of Biochemical Pharmacology, Hypertension-Endocrine Branch, National Heart and Lung Institute, Bethesda, MD 20014 **Induction of tyrosine hydroxylase in the superior cervical ganglia of rats: opposite influence of muscarinic and nicotinic receptor agonists.** Neuropharmacology (Oxford). 15(2):85-90, 1976.

The opposite influences of muscarinic and nicotinic receptor agonists on induction of tyrosine hydroxylase in the superior cervical ganglia of rats are reported. Nicotine induced tyrosine hydroxylase in superior cervical ganglia. This action was facilitated by a blockade of muscarinic receptors and inhibited by an activation of these receptors. In ganglia, an endogenous store of catecholamines which was released by muscarinic receptor agonists, mediated the inhibition of tyrosine hydroxylase induction elicited by methacholine. Since apomorphine inhibited the tyrosine hydroxylase induction by nicotine or reserpine, but methacholine only inhibited the action of nicotine, it is suggested that the inhibition of tyrosine hydroxylase induction elicited by methacholine was mediated by dopamine. Nicotine failed to induce tyrosine hydroxylase in decentralized ganglia. When atropine was associated with nicotine, the latter also induced tyrosine hydroxylase in decentralized ganglia. It is concluded that activation of muscarinic and nicotinic receptors exerts a mutually antagonistic influence in the control of tyrosine hydroxylase biosynthesis in sympathetic ganglia. 25 references. (Author abstract)

239982 Polzin, R.; Barnes, C. D. Dept. of Life Sciences, Indiana State Univ., Terre Haute, IN 47809 **The effect of diazepam and picrotoxin on brainstem evoked dorsal root potentials.** Neuropharmacology (Oxford). 15(2):133-137, 1976.

The effects of diazepam and picrotoxin on brainstem evoked dorsal root potentials were investigated. Experiments were performed on cats made decerebrate at the precollicular level. Dorsal root potentials were recorded from the most caudal rootlet of L6 or L7 and the monosynaptic reflex was recorded from the ventral root of L7. Stimulation was either a single shock to the gastrocnemius soleus or common peroneal nerve or a 20 msec train at 500Hz to sites in the brainstem reticular formation. The initial negative dorsal root potentials were enhanced by diazepam regardless of origin. Diazepam also enhanced positive dorsal root potentials from the pontine reticular formation. Some pure positive dorsal root potentials from the caudal medullary reticular formation were depressed by diazepam. Picrotoxin was always found, even when diazepam depressed dorsal root potentials, to have the antagonistic action of diazepam; i.e.,usually depressing the negative or positive supraspinal dorsal root potential. 19 references. (Author abstract)

240063 Costall, Brenda; Naylor, Robert J.; Pycock, Chris. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, West Yorkshire, England **Non-specific supersensitivity of striatal dopamine receptors after 6-hydroxydopamine lesion of the nigrostriatal pathway.** European Journal of Pharmacology (Amsterdam). 35(2):275-283, 1976.

The effect of 6-hydroxydopamine (6-OHDA) lesions of the nigrostriatal pathway on sensitivity of striatal dopamine receptors was studied by injecting 6-OHDA unilaterally into the area of the ascending dopamine pathways in the lateral hypothalamus of rats. Results indicate that after 6-OHDA induced degeneration of the nigrostriatal dopamine system, there are changes in sensitivity of striatal mechanisms to dopamine, noradrenaline and 5-hydroxytryptamine to evoke an enhanced circling or contralateral asymmetric behavior. The 6-OHDA also enhances the abilities of both dopamine and noradrenaline to induce contralateral forelimb dyskinesias. It is suggested that an interpretation of the enhanced response to apomorphine and similar agents after peripheral administration to animals with 6-OHDA lesions may require a consideration of changes in receptor specificity in addition to supersensitivity. 21 references.

240064 Gerold, Marcel; Cavero, Icilio; Riggenbach, Hans; Wall, Michael; Haeusler, Gunther. Department of Experimental Medicine, T. Hoffmann-La Roche & Co., Ltd., Basle, Switzerland **Analysis of cardiac chronotropic responses to diazepam and bromazepam in conscious trained dogs.** European Journal of Pharmacology (Amsterdam). 35(2):361-368, 1976.

Cardiac chronotropic effects of bromazepam and diazepam were measured in conscious trained dogs. Administration of bromazepam (0.3mg/kg) or diazepam (0.3and 1.0mg/kg) was found to have no influence on heartrate. A higher dose (10mg/kg) of the two drugs elicited a positive chronotropic effect which was rapid in onset and of long duration. The beta adrenoreceptor blocking agent practolol (2.5mg/kg) did not revert heartrate after the benzodiazepines to the same level as in controls, indicating that the tachycardia was not produced by an increase in sympathetic outflow to the heart. For diazepam, a sympathetic/parasympathetic interaction cannot be excluded. However, diazepam and bromazepam significantly reduced the tachycardia which is normally observed after administration of methylatropine alone or in combination with practolol. In anesthetized dogs, bromazepam failed to modify the heartrate responses to electrical stimulation of cardiac vagal or sympathetic nerves, excluding an action of this compound on ganglionic transmission and cardiac cholinoceptors and adrenoceptors. 18 references. (Author abstract modified)

240065 Hudick, James P.; Wajda, Isabel J.; Lajtha, Abel. New York State Research Institute for Neurochemistry and Drug Addiction, Ward's Island, New York, NY 10035 **The amphetamine-induced inhibition of dopamine biosynthesis in rat striatum.** European Journal of Pharmacology (Amsterdam). 35(2):389-392, 1976.

In a postnatal developmental study of dopamine biosynthesis in rat striatum, the dopamine biosynthetic machinery of intact synaptosomes of rat striatum showed a five fold increase in development from 3-day-old neonates to adults. It was fully developed betwen 2 and 3 weeks after birth. Concurring with this development was the appearance 2 weeks after birth of a regulatory mechanism through which amphetamine in vivo induced an inhibition of dopamine biosynthesis. The inhibition was not appreciably reversed when haloperidol in addition to amphetamine, was administered. 9 references. (Author abstract modified)

240073 Aghajanian, George K.; Haigler, Henry J. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Hallucinogenic indoleamines: preferential action upon presynaptic serotonin receptors.** Psychopharmacology Communications. 1(6):619-629, 1975.

Preferential action of hallucinogenic indoleamines on presynaptic serotonin receptors is described. Using microiontophoretic techniques, the relative potencies of three indoleamine hallucinogens, psilocin, dimethyltryptamine (DMT) and bufotenine were tested upon serotonin neurons in the raphe (presynaptic neurons) and postsynaptic neurons in the ventral lateral geniculate and amygdala of the rat. Psilocin showed the greatest preferential inhibitory effect upon raphe as compared to postsynaptic neurons. DMT was intermediate, and bufotenine had the least differential activity. This rank ordering correlates with the relative hallucinogenic potencies of these compounds: psilocin is greater than DMT which is greater than bufotenine. The results support the hypothesis that low doses of indoleamine hallucinogens act preferentially upon presynaptic serotonin receptors to inhibit raphe neurons, thus releasing postsynaptic neurons from a tonic inhibitory serotonergic influence. 24 references. (Author abstract modified)

240077 Snyder, Solomon H.; Creese, Ian; Burt, David R. Dept. of Pharmacology and Experimental Therapeutics, Johns Hopkins Univ. School of Medicine, Baltimore, MD 21205 **The brain's dopamine receptor: labeling with (3H)dopamine and (3H)haloperidol.** Psychopharmacology Communications. 1(6):663-673, 1975.

Labeling of the dopamine receptor site of the brain with (3H)dopamine and (3H)haloperidol is discussed. The importance of ensuring that the binding of dopamine and haloperidol involves physiologically relevant postsynaptic dopamine receptors is emphasized, and evidence from regional variations and drug specificity studies is presented. It is shown that (3H)dopamine and (3H)haloperidol display similar specificity for many drugs and appear to be labeling the same or related sites. Quantitative differences between these sites and in the potencies of different drugs are explained using a two state model of receptor action. Clinical implications of the relative effects of different drugs on dopamine receptors in different brain areas are outlined. To ensure that dopamine receptor binding involves postsynaptic sites rather than sites on nerve terminals of dopamine neurons, the influence of unilateral destruction of the nigrostriatal dopamine pathway was examined. 19 references.

240238 Nowak, Jerzy Z.; Pilc, Andrzej. Centrum Badan Molekularnych i Makromolekularnych PAN, 90-136 Lodz, Narutowicza 60, Poland **The influence of mepyramine and burimamide on histamine induced catalepsy in the rat.** Acta Physiologica Polonica (Warszawa). 26(5):529-532, 1975.

The influence of mepyramine and burimamide on histamine induced catalepsy was examined in the rat. Catalepsy was induced in albino Wistar rats by injection of histamine (Hi). Mepyramine, the specific inhibitor of H1 Hi receptors, and burimamide, the specific blocker of H2 Hi recpetors, were injected into the rats to determine whether these inhibitors of Hi receptors would modulate post-Hi catalepsy in rats. Mepyramine injected intraperitoneally antagonized post-Hi catalepsy, and burimamide given into the right ventricle of the brain potentiated the cataleptic action of Hi. It is supposed that Hi, involving H1 receptors, produces catalepsy indirectly, probably through dopaminergic system in striatum. 21 references. (Author abstract modified)

240240 Kruszewska, Alicja. Zaklad Farmakodynamiki Instytutu Patologii Klinicznej AM, 20-081 Lublin, Staszica 4, Poland **Central action of normetanephrine. Effect on the behavior of rats.** Acta Physiologica Polonica (Warszawa). 26(6):583-590, 1975.

The effects of intraventricular normetanephrine (NM) on the central nervous system of Wistar rats were studied. It was found that NM in low doses increases and in high doses decreases the spontaneous motor activity. In the dose of 12.5micrograms, NM raised the body temperature, slightly prolonged the duration of pain reaction, shortened the duration of general anesthesia induced with chloralhydrate, and increased fluphenazine induced catalepsy. The dose of 0.4mg reduced the cognitive activity, caused hypothermia, prolonged slightly the duration of pain reduction, disturbed motor coordination, increased the intensity of seizures evoked by electric shock, prolonged the time of general anesthesia produced with hexobarbital and ethanol, and increased the intensity of fluphenazine catalepsy. Thus, NM exerted a two stage effect on the central nervous system: a weak stimulatory one after small doses and an inhibitory one after high doses. 29 references. (Author abstract)

240242 Hoffer, B. J.; Freedman, R.; Woodward, D. J.; Daly, J. W.; Skolnick, P. Lab. of Neuropharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Beta-adrenergic-control of cyclic AMP-generating systems in cerebellum: pharmacological heterogeneity confirmed by destruction of interneurons. (Unpublished paper).** Washington, DC, NIMH, 1976. 25 p.

The electrophysiological and neurochemical interaction of neuroleptic compounds with the beta-adrenergically linked cyclic adenosine-3′,5′-monophosphate (AMP) generating systems of cerebellum was examined in rats. Intracisternal injection of 6-hydroxydopamine (6-OHDA) to X-irradiated animals resulted in an 80% increase in Purkinje cell mean discharge rate, suggesting an inhibiting adrenergic input comparable to that seen in normal animals. Iontophoresis of fluphenazine reversed the inhibitory effects of iontophoretically applied norepinephrine (NE) on Purkinje cell discharge rate in both X-irradiated animals and X-irradiated animals treated with 6-OHDA. The NE stimulated formation of cyclic-AMP was significantly reduced in cerebellar slices prepared from X-irradiated rats as compared with controls. While fluphenazine reduced the NE stimulated formation of cyclic-AMP by 50-60% in cerebellar slices from control rats, the same concentration of fluphenazine reduced NE elicited accumulation of cyclic-AMP to values which were not significantly different from basal values in slices from X-irradiated rats. 28 references. (Author abstract modified)

240447 Kiessling, Marika; Lindl, Toni; Cramer, Hinrich. Neurologische Klinik, Hansastrasse 9, D-7800 Freiburg i. Br., Germany **Cyclic adenosinemonophosphate in cerebrospinal fluid: effects of theophylline, L-Dopa and a dopamine receptor stimulant in rats.** Archiv fur Psychiatrie und Nervenkrankheiten (Berlin). 220(4):325-333, 1975.

The effects of L-dopa and the dopamine receptor stimulant ET-495 (Piribedil) on cisternal cyclic adenosine monophosphate (cAMP) levels were studied in rats. L-Dopa (100-200mg/kg) increased the cisternal cAMP levels by 60% to 80%. When peripheral dopa-decarboxylase was inhibited, smaller doses of L-dopa were effective. Fla-63 (bis-(4-methyl-1-homopiperazinyl thiocarbonyl)-disulfide), an inhibitor of dopamine-beta-hydroxylase, lowered the increase induced by L-dopa which was completely suppressed by propranolol, but not by phentolamine. This suggests that the cisternal cAMP increase was mediated through a central beta-adrenoceptor stimulation. ET-495 failed to influence cisternal cAMP levels, arguing against a dopamine sensitive adenylate cyclase involved in the L-dopa effect. Moreover, large increases of cisternal cAMP levels were observed after treatment with theophylline, but not papaverine, which suggests different effects of these phosphodiesterase inhibitors. 26 references. (Author abstract)

240474 Vazquez, Alfredo J.; Diamond, Bruce I.; Sabelli, Hector C. Dept. of Anesthesiology, Mount Sinai Hospital, Chicago, IL 60612 **Differential effects of phenobarbital and pentobarbital on isolated nervous tissue.** Epilepsia (Amsterdam). 16(4):601-608, 1975.

Epileptiform afterdischarges evoked by repetitive electrical stimulation of chronically isolated cortical slabs (cat) were shortened by low doses of phenobarbital but were not affected by hypnotic doses of pentobarbital. Both pentobarbital and phenobarbital raised threshold and lowered spike amplitude in isolated sciatic nerves. The action of both drugs was increased by reducing sodium in the medium and by decreasing the Ringer's pH. Similar to the action of other general anesthetics, the axonal effect of pentobarbital was enhanced by deuterium oxide (D2O) replacement for water in the Ringer's (suggesting that tissue water is involved in pentobarbital action), whereas D2O replacement did not modify the action of phenobarbital or of local anesthetics. These results suggest that the varying in vivo effects of pentobarbital and phenobarbital may be due to a difference in their action upon excitable membranes (rather than to a different regional distribution in brain). 36 references. (Author abstract)

240523 Steiner, F. A.; Felix, D. Institute for Brain Research, University of Zurich, 8029 Zurich, Switzerland **Antagonistic effects of GABA and benzodiazepines on vestibular and cerebellar neurones.** Nature (London). 260(5549):346-347, 1976.

The hypothesis that the benzodiazepines act through a facilitation of gamma-amminobutyric acid (GABA) mediated transmission was tested electrophysiologically at the single unit level in the lateral vestibular nucleus (Deiters) of the cat and in Purkinje cells of the cerebellum of rats, areas where GABA is known to act as an inhibitory transmitter. Results indicate a functional antagonism between benzodiazepines and GABA. In both systems studied, inhibitory GABA influences were suppressed in a dose dependent manner by benzodiazepines; this effect could be reversed by increasing local GABA concentrations through stimulation of the appropriate axons or through microiontophoretic delivery of GABA. The effect of the specific GABA antagonist, bicuculline, was not impaired by benzodiazepines. It is concluded that these results contradict the GABA facilitation hypothesis for benzodiazepines, as GABA mediated inhibition on Deiters neurons and Purkinje cells was clearly antagonized by these drugs. 14 references.

240642 Riegle, G. D.; Meites, J. Dept. of Physiology, Michigan State University, East Lansing, MI 48824 **Effects of aging on LH and prolactin after LHRH L-dopa, methyl-dopa, and stress in male rat.** Proceedings of the Society for Experimental Biology and Medicine. 151(3):507-511, 1976.

Hypothalamic pituitary control of prolactin and luteinizing hormone (LH) secretion was tested in young (4-6 months) and aged (22-30 months) male Long-Evans rats given L-dopa, methyl dopa, LH releasing hormone (LHRH), or stress treatments. Pretreatment serum LH levels were consistently higher in young than in the aged groups. The increase in serum LH after LHRH injection was only about half as much in aged as compared to young control males. Although acute stress caused a prompt increase in serum LH in young male rats, this treatment was without effect in the aged group. Methyl dopa

treatment stimulated serum prolactin secretion in both young and old rats. Although L-dopa treatment caused a reduction in serum prolactin in both age groups, the sensitivity, magnitude, and duration of the reduction was smaller in the aged rats. 15 references. (Author abstract modified)

240643 Gil-ad, Irit; Zambotti, Fernanda; Carruba, Michele O.; Vicentini, Lucia; Muller, Eugenio E. Dept. of Pharmacology, University of Milan, Milan 20129, Italy **Stimulatory role for brain serotoninergic system on prolactin secretion in the male rat.** Proceedings of the Society for Experimental Biology and Medicine. 151(3):512-518, 1976.

The effect of acute or chronic functional ablation of the central serotonergic system on circulating plasma prolactin levels was investigated in the rat by using pharmacological agents which specifically affect brain serotonin (5-HT) neurons or by limiting the amount of the 5-HT precursor amino acid, tryptophan, in the diet. Systemic administration of parachlorophenylalanine, a blocker of 5-HT synthesis, considerably decreased brain 5-HT and plasma prolactin levels in young male rats. Intraventricular administration of 5,7-dihydroxytryptamine, a neurotoxic drug which destroys 5-HT nerve terminals, induced a marked depletion of brain 5-HT and 5-hydroxyindoleacetic acid (5-HIAA) and considerably reduced plasma prolactin levels at 3, 12, and 30 days after treatment. A tryptophan deficient diet, for up to 4 days, caused a depletion of brain 5-HT and 5-HIAA contents and did not modify prolactin levels. Addition of tryptophan to this diet reversed the 5-HT and 5-HIAA depletion and significantly increased prolactin levels. These data provide evidence for the role of the serotonergic system in the maintenance of tonic prolactin secretion. 31 references. (Author abstract modified)

240699 Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Some recent advances in the biochemical pharmacology of gamma-aminobutyric acid (GABA). (Unpublished paper).** Washington, DC, NIMH, 1976. 26 p.

Three tangential issues in biochemical pharmacology which relate to the role of gamma-aminobutryic acid (GABA) as a tool in psychiatric research are discussed. Evidence is presented that GABA participates in the action of anxiolytic benzodiazepines. Some aspects of the pharmacological action of muscimol are described, which indicate that this drug may act in vivo as a potent GABA receptor agonist. Consideration is given to the measurement of turnover rate of GABA in substantia nigra, striatum and nucleus accumbens of rats. 40 references.

240740 Lehmann, Karla. Institut fur Pharmakologie und Toxikologie, 801 Dresden, Lingerplatz 1, Germany **/On the mechanisms of action and kinetics of lithium./** Zum Wirkungsmechanismus und zur Kinetik von Lithium. Psychiatrie, Neurologie und Medizinische Psychologie (Leipzig). 27(12):705-719, 1975.

Biochemical and pharmacodynamic effects of lithium (Li-) were examined in an attempt to explain lithium's general mechanism of action. It proposed that Li- may affect the activity of membrane bound adenosine triphosphatase, depending on the initial situation, dose, and duration of application. It is also suggested that active processes participate in the transport of the ion through the organism. The distribution of Li-within a multiple component system is described, which is, with the exception of the resorption phase, independent of the anion used. It is also stated that the elimination is limited by backward flow from the tissues. 61 references. (Journal abstract modified)

240746 DeLorenzo, Robert J.; Glaser, Gilbert H. Dept. of Neurology, Yale University School of Medicine, New Haven, CT 06510 **Effect of diphenylhydantoin on the endogenous phosphorylation of brain protein.** Brain Research (Amsterdam). 105(2):381-386, 1976.

The effect of diphenylhydantoin (DPH) on endogenous brain protein phosphorylation was investigated in rat cerebellum. Results indicate that DPH caused a substantial decrease in the amount of (32P)phosphate incorporated into a specific radioactive band seen in the autoradiograph and the scintillation counting of gel slices. This radioactive band was subsequently demonstrated to be associated with (32p)phosphoprotein. The direct effect of DPH on the level of phosphorylation of this brain protein suggests that the enzymes responsible for controlling the net level of phosphorylation of this protein may be affected by DPH. The net decrease in the level of phosphorylation of a protein substrate caused by DPH could result either from a DPH induced decrease in the activity of a specific protein kinase or from a DPH induced increase in the activity of a specific protein phosphatase, or both. It is suggested that the effect of DPH on protein phosphorylation may play an important role in mediating the stabilizing actions of the anticonvulsant on neuronal activity and seizure discharge. 15 references.

240886 Houser, Vincent P. RD 1, Box B95, Rt. 94, Chester, NY 10918 **Effects of haloperidol on aversive threshold of rats.** Psychological Reports. 38(1):115-118, 1976.

The analgesic potency of haloperidol (.15, .30, 2.5, 5.0mg/kg) in the rat was assayed, using the spatial preference technique. This drug was able to raise the aversive threshold in a dose dependent manner in doses at or above .15mg/kg. These same dosages also significantly reduce the number of motor responses made during threshold testing. These results are interpreted to suggest that haloperidol produces its effects on the aversive threshold indirectly by inhibiting the execution of the escape response. 5 references. (Author abstract)

240933 Chung, Ho. University of Maryland Baltimore Professional School **The effect of ethanol-stress in combination on the pharmacologic action of hexobarbital. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. Microfilms, No. 75-29356 HC$18.00 MF$7.50 87 p.

The effect of the combination of ethanol and stress on drug action and its biochemical basis were studied in male rats. It was found that ethanol (3g/kg orally) and stress (unilateral and hind leg ligature) individually caused a significant inhibition in hexobarbital metabolism, and an additive effect resulted from their combination. A dose/response relationship occurred for the inhibition of hexobarbital metabolism by ethanol, and a time/response relationship occurred for inhibition by acute stress. The microsomal metabolism of hexobarbital was decreased by both treatments. No evidence for an inhibitor of microsomal metabolism in the cytosol occurred, nor was microsomal protein level affected. However, microsomal cytochrome P-450 levels were significantly reduced by both treatments. Acute ethanol and acute stress alone increased plasma level of corticosterone significantly, and the combined treatment had an additive effect on corticosterone release which was absent in adrenalectomized rats. No inhibition of hexobarbital metabolism in adrenalectomized rats occurred under either acute condition. Results indicate that hexobarbital sleep time was not a good indicator of drug metabolism. Stress reduction of the amount of the drug reaching the systemic circulation and the central nervous system depressant effect of ethanol may explain this observation. Findings show that the

inhibitory effect of alcohol and/or stress on hexobarbital metabolism is associated with corticosterone release, which may serve as an alternate substrate for hexobarbital in the hepatic microsomal mixed function of oxidase system. (Journal abstract modified)

240934 Gorodetzky, Charles William. University of Kentucky **Drug receptor interactions of morphine and nalorphine: competitive dualism versus receptor dualism. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-26454 HC$18.00 MF$7.50 164 p.

The effects of morphine alone (four doses), nalorphine alone (six doses), morphine plus nalorphine in combination (16 drug conditions) and saline placebo (four administrations) were studied to differentiate between the two major hypotheses for opiate/opiate antagonist receptor interaction (competitive dualism and receptor dualism). A test system was developed in which a suprathreshold electrical stimulus was applied to the soft tissues of the mouth of an intact rabbit. The resulting chewing activity was quantitatively evaluated by counting peaks on a polygraph record produced by movement in electrodes hanging from the foliate papillae on the floor of the mouth. Drug effects were measured as percent depression of chewing activity compared to predrug control, evaluated at 20, 40, and 60 minutes following intravenous drug administration. Although results did not differentiate between the two hypothesized receptor models, statistical techniques were developed to estimate some of the parameters of drug receptor interaction, including a measure of variability. Using these techniques a direct kinetic approach to the study of drug receptor interaction is demonstrated which could become a valuable addition to the multiple approaches which have been used to study this problem. (Journal abstract modified)

240936 Quock, Raymond Mark. University of Washington **Apomorphine-induced hyperthermia in the rabbit: a pharmacological study of the neuroaminergic mechanisms underlying the response. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-28423 HC$18.00 MF$7.50. 232 p.

The influence of the dopaminergic agonist apomorphine on the body temperature of the rabbit was investigated. Apomorphine elevated the colonic temperature of stanchion restrained Ss in a dose related manner. Concomitant drug effects included locomotor hyperactivity, stereotyped behavior (compulsive gnawing), dilatation of ear vasculature, increased respiration, mydriasis and increases in ear and torso skin temperatures. These responses were competitively inhibited by pimozide, a dopaminergic antagonist. Overall results of experiments indicate that apomorphine possesses thermotropic activity that is mediated through the central nervous system. A hyperthermic response originates from the activation of dopaminergic receptors in the preoptic anterior hypothalamic region. Serotonergic and alpha adrenergic mediatory components also participate in the neurogenesis of the hyperthermic response. A hypothermic response originates from the activation in the vicinity of the caudal third ventricle of a nondopaminergic, nonserotonergic heat dissipating mechanism. It is unlikely that d-amphetamine, an indirect acting dopaminergic stimulant, acts upon the same neuronal substrates to elicit central actions superficially similar to the effects of apomorphine. (Journal abstract modified)

241100 Lewis, Michael James. Temple University **Reduction in morphine tolerance and physical dependence and opioid-seeking behavior by intracerebral 6-hydroxydopamine. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-28182 HC$18.00 MF$7.50 49 p.

The effects of intracerebral 6-hydroxydopamine injections on morphine tolerance and physical dependence, as well as on opioid seeking behavior were assessed in animals. Bilateral destruction of the ventral noradrenergic bundle by direct injection of the compound selectively depleted forebrain areas of norepinephrine. Maximum depletion occurred in the hypothalamus and the dorsal diencephalon. This treatment reduced tolerance to injection of morphine, reduced the symptoms of abstinence and precipitated withdrawal. Finally, it reduced the voluntary consumption of opioids, suggesting that hypothalamic and diencephalic norepinephrine are responsible in part for the phenomena of opioid seeking behavior, tolerance, and physical dependence. (Journal abstract modified)

241129 Stone, Jonathan. New York University **An analysis of the double-pulse technique's use in measuring hypothalamic refractory periods in reward neurons. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-28599 HC$18.00 MF$7.50 188 p.

The usefulness of the double pulse technique in measuring hypothalamic refractory periods (RPs) in reward neurons was assessed in three experiments with rats to determine from the shape of the refractory recovery curve whether or not fibers of one or more diameter size mediate the electrically elicited self-reward. Three currents at which to test the shape were determined for each S (high, low, or medium). At each of these currents, a large number of intrapair intervals spanning the RP range were systematically sampled. DFP and imipramine, respectively prolonging cholinergic and adrenergic transmitter action, were used to alter responding at different segments of the refractory recovery curve. In the course of current determination in experiment one, it was found that the current effectiveness ranges for the Ss differed in terms of length and shape. In experiment two, the higher the current at which the RP measurements were done, the shorter the intrapair pulse interval at which recovery from refractoriness commenced, suggesting that recovery from relative refractoriness was being manipulated by current changes. In addition, synaptic amplification factors were probably involved. In experiment three, the drugs had only weak effects on RP recovery rates. Low, but not high doses of imipramine, significantly facilitated responding, but DFP had an inhibitory effect that may not have been specific to the self-stimulation system. (Journal abstract modified)

241196 Sachs, Charlotte; Jonsson, Gosta. Department of Histologgy, Karolinska Institute, S-104 01 Stockholm, Sweden **Effects of 6-hydroxydopamine on central noradrenaline neurons during ontogeny.** Brain Research (Amsterdam). 99:277-291, 1975.

The effects of the catecholamine neurotoxic compound, 6-hydroxydopamine (6-OHDA) were investigated on central noradrenaline (NA) neurons after neonatal administration in rats. This treatment led to a pronounced reduction of the in vitro uptake of (3H)NA and the endogenous NA in the cerebral cortex, while these parameters were markedly augmented in the pons and medulla oblongata, regions containing the NA perikarya. The 6-OHDA induced changes in the cerebral cortex and the pons medulla could be completely prevented by the membrane pump blocker desipramine, indicating that the effects are associated with a specific pons medulla from 6-OHDA treated rats had the same kinetic and pharmacological properties as that of control. Thus the ob-

served differences in (3H)NA uptake are most likely quantitatively related to actual changes in the number of NA nerve terminals. Treatment with lower 6-OHDA doses resulted in less pronounced reduction of (3H)NA uptake initially, and there was a gradual recovery of uptake with time in the cerebral cortex, which was more pronounced after the lower dose. These results are indications of regenerative growth, which may be possible when a critical part of the axon is spared from the neurotoxic effect of 6-OHDA. 38 references. (Author abstract modified)

241203 Rastogi, R. B.; Lapierre, Y.; Singhal, R. L. Dept. of Pharmacology, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada **Evidence for the role of brain biogenic amines in depressed motor activity seen in chemically thyroidectomized rats.** Journal of Neurochemistry (Oxford). 26(3):443-449, 1976.

The effects of exposure to an antithyroid drug, methimazole, on brain tyrosine hydroxylase and tryptophan hydroxylase activity, as well as the levels of norepinephrine, dopamine, 5-hydroxytryptamine and 5-hydroxyindoleacetic acid were investigated in maturing rat brain. The activities of brain tyrosine hydroxylase and tryptophan hydroxylase and the levels of norepinephrine, dopamine and 5-hydroxytryptamine were markedly altered in a dose and time dependent manner in methimazole treated rats. The concentration of brain 5-hydroxyindoleacetic acid was elevated (46%) by methimazole administration. Administration of triiodothyronine to hypothyroid rats for 30 days did not produce any appreciable effect upon the neurochemical parameters related to either norepinephrine or 5-hydroxytryptamine metabolism. However, increasing the dose of triiodothyronine significantly elevated the levels of norepinephrine and 5-hydroxytryptamine as well as the activities of the two synthesizing enzymes, tyrosine hydroxylase and tryptophan hydroxylase. Brain 5-hydroxyindoleacetic acid levels were restored to normal values in thyroid hormone deficient rats treated with this higher dose of triiodothyronine. Evidence also was obtained to show that chemical thyroidectomy suppressed the spontaneous locomotor activity in neonatal rats. The data support the view that thyroid hormone in neonatal life displays an important regulatory effect on the metabolism of norepinephrine, dopamine and 5-hydroxytryptamine. 37 references. (Author abstract modified)

241206 De Belleroche, J. S.; Bradford, H. F.; Jones, D. G. Dept. of Biochemistry, Imperial College of Science and Technology, Prince Consort Rd., London, S.W. 7, England **A study of the metabolism and release of dopamine and amino acids from nerve endings isolated from sheep corpus striatum.** Journal of Neurochemistry (Oxford). 26(3):561-571, 1976.

The metabolic compartmentation and release of dopamine synthesized endogenously in isolated striatal nerve endings were examined and compared to the actions of releasing agents such as electrical pulses and amphetamine. Synaptosomes prepared from sheep corpus striatum showed a linear rate of respiration over a 90 minute period of incubation, and the rate of respiration was stimulated by electrical pulses. Dopamine was released from synaptosome beds to the medium by either electrical pulses or potassium ion, increasing 108% and 76%, respectively, above control levels of release. The presence of d-amphetamine of l-amphetamine in the incubation medium increased the accumulation of dopamine in the medium by 310% and 275%, respectively, and potassium ion also caused a significant increase in the release of glutamate, gamma-aminobutyric acid (GABA) and aspartate. Radioactively labeled dopamine was synthesized by the synaptosomes from L-(14C)tyrosine, L-dopa or DL-dopa, and electrical pulses caused a 35% increase in the rate of dopamine production from (U-14C)tyrosine. In the presence of l-amphetamine and d-amphetamine, accumulation of 14C-labeled dopamine in the incubation media was increased 129% and 380%, respectively; the latter was partially depressed by absence of calcium from the medium. It is proposed that one pool of dopamine is released by depolarizing agents and during the period of incubation is replaced by synthesis from the endogenous tyrosine and not by the labeled dopamine in the synaptosome. The synaptosomal pool of dopamine which is radioactively labeled after pulse labeling with DL-(2-14C)dopa appears to be prone to oxidation to 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid which are preferentially released from the synaptosomes. 50 references. (Author abstract modified)

241207 Korf, J.; Grasdijk, L.; Westerink, B. H. C. Dept. of Biological Psychiatry, Psychiatric University Clinic, Oostersingel 59, Groningen, The Netherlands **Effects of electrical stimulation of the nigrostriatal pathway of the rat on dopamine metabolism.** Journal of Neurochemistry (Oxford). 26(3):579-584, 1976.

The effects of electrical stimulation of the nigrostriatal dopaminergic pathway in rat brain were examined. Stimulation elicited a frequency and current intensity dependent increase in the formation of homovanillic acid in the basal ganglia. The accumulation of the acid in probenecid treated animals was constant over one hour when maximally stimulated at 25 Hz. Dopamine levels remained unchanged during stimulation. When prior to stimulation the inhibitor of catecholamine synthesis alpha-methyl-p-tyrosine methyl ester was administered, dopamine levels declined biphasically. Tyrosine and nomifensine, a dopamine uptake inhibitor, and apomorphine had no major effect on the formation of homovanillic acid, while alpha-methyl-p-tyrosine prevented its formation. The data suggest that dopamine in the striatum is compartmentalized and that the newly synthesized amine is released and converted to homovanillic acid. Apomorphine decreases dopamine flux only when dopaminergic neurons are at rest. When depolarized, neither access of the precursor nor reuptake seem to influence the conversion of dopamine to homovanillic acid. 44 references. (Author abstract)

241208 Saavedra, J. M. Section of Pharmacology, Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **5-Hydroxy-L-tryptophan decarboxylase activity: microassay and distribution in discrete rat brain nuclei.** Journal of Neurochemistry (Oxford). 26(3):585-589, 1976.

5-Hydroxy-L-tryptophan decarboxylase activity was measured in discrete regions of the rat brain by means of a sensitive micromethod that allows the quantitation of enzyme activity in very small amounts of brain tissue. A good correlation was obtained between serotonin levels and 5-hydroxy-L-tryptophan decarboxylase activity in all the brain regions examined. Wide differences in enzyme activity were found in the different brain nuclei, with a 20 fold difference in activity between the most active region (the nucleus raphe dorsalis) and the least active regions (the corpus callosum and the optic tract). 18 references. (Author abstract)

241222 Noble, E. P.; Gillies, R.; Vigran, R.; Mandel, P. Div of Neurochemistry, Department of Psychiatry and Human Behavior, University of California, Irvien, CA 92664 **The modification of the ethanol withdrawal syndrome in rats by di-n-propylacetate.** Psychopharmacologia (Berlin). 46(2):127-131, 1976.

The effects of di-n-propylacetate (DPA), a drug known to increase brain gamma-aminobutyric acid (GABA) levels and to inhibit GABA transaminase (GABA-T) activity administered during the ethanol withdrawal period to rats made physically dependent upon ethanol were examined. Under all conditions tested, 400mg DPA/kg injected i.p. significantly reduced the withdrawal hyperexcitable state induced by acoustic stimulation. The effect was seen as early as 30 min after the administration of DPA and lasted for at least 2 hrs. Readministration of the same dose of DPA 6.5hrs after its initial injection again mitigated withdrawal symptoms. A 200mg/kg dose of DPA was significantly effective for only 1 hr after its administration. Neither dose led to mortality or observable tranquilization. The results suggest that DPA may be a useful agent in the control of the hyperexcitable state induced by ethanol withdrawal, and that the GABA system may be involved in this state. 27 references. (Author abstract)

241232 Stock, G.; Heinemann, H.; Bergande, F. Department of Physiology, University of Heidelberg, D-6900 Heidelberg, Im Neuenheimer Feld 326, Germany **Changes in excitability of amygdaloid and septal nuclei induced by medazepam hydrochloride.** Psychopharmacologia (Berlin). 46(2):197-203, 1976.

Changes in the excitability of amygdaloid and septal nuclei induced by medazepam hydrochloride were examined in the cat. Medazepam hydrochloride attenuated slightly the cardiovascular reactions and elevated markedly the thresholds for psychomotor behavior. The latencies between the onset of electrical stimulation and the beginning of the increase in arterial pressure were only slightly increased, whereas the latencies for psychomotor behavior were markedly prolonged due to drug application. The data support the view that medazepam hydrochloride exerts depressant effects on the limbic hypothalamic level with respect to psychomotor responses. The effect was not identical for all nuclei tested. The basolateral part of the amygdala was significantly less sensitive to medazepam hydrochloride than the central part fo the amygdala. 33 references. (Author abstract modified)

241235 Samanin, R.; Bernasconi, S.; Quattrone, A. Istituto de Ricerche Farmacologiche "Mario Negri", Lab. of Neuropharmacology, Via Eritea 62, I-20157, Milan, Italy **Antinociceptive action of quipazine: relation to central serotonergic receptor stimulation.** Psychopharmacologia (Berlin). 46(2):219-222, 1976.

Quipazine, a serotonin receptor stimulant, inhibited the response of rats to painful stimuli in two methods used to measure antinociception in these animals. The antinociceptive action was observed with doses ranging from 5-20mg/kg i.p. according to the test situation. The effect was significantly antagonized by a pretreatment with methergoline, a potent serotonin antagonist. An electrolytic lesion placed in the nucleus raphe medianus, which produced a marked decrease of serotonin in the forebrain did not, or only slightly affected the effect of quipazine, depending on the method used to measure antinocinception. It is suggested that quipazine can produce antinociceptive action in rats by interacting with a serotonergic mechanism. It is felt that the action is due mainly to a direct effect on postsynaptic serotonin receptors, although a presynaptic component may also contribute to the effect of quipazine. 24 references. (Author abstract modified)

241242 Magour, Samir; Coper, Helmut; Fahndrich, Christa; Hill, Regina. Institute of Neuropsychopharmacology, Free University of Berlin, Ulmenallee 30, D-1000 Berlin 19, Germany **Relationship between the subcellular distribution of delta9-tetrahydrocannabinol and its metabolites in rat brain and the duration of the effect on motor activity.** Life Sciences (Oxford). 18(6):575-584, 1976.

The relationship between the subcellular distribution of delta9- tetrahydrocannabinol(delta9-THC) and its metabolites in rat brain and the duration of the effect on motor activity were investigated. In female rats injected with delta9-THC, the maximum depressant effect on locomotor activity was observed between the first and fourth hour and had completely disappeared by the eighth hour of treatment. In parallel experiments rats were injected with 3H-delta9-THC and decapitated either 1, 4, or 12 hours later. There were no substantial differences in the relative specific activities of delta9-THC or 11-OH-delta9-THC between all fractions except cytosol, indicating no preferential site of accumulation. However, when the synaptosomal fraction was osmotically shocked, the concentration of delta9-THC in nerve ending membranes was markedly higher than that in vesicles or soluble fraction. Results in vivo show a marked decline over 12 hours in the relative specific activities of delta9-THC and 11-OH-delta9-THC with a concomitant increase in the concentration of highly polar, nonextractable metabolites in all subfractions. 17 references. (Author abstract modified)

241246 Opmeer, F. A.; Gumulka, S. W.; Dinnendahl, V.; Schonhofer, P. S. Institut for Pharmakologie, Medizinische Hochschule Hannover, Karl-Wiechert-Allee 9, D-3000 Hannover 61, Germany **Effects of stimulatory and depressant drugs on cyclic guanosine 3',5'-monophosphate and adenosine 3',5'-monophosphate levels in mouse brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 292(3):259-265, 1976.

The effects of stimulatory and depressant drugs on cyclic quanosine-3',5'-monophosphate (GMP) and cyclic adenosine-3',5'-monophosphate (cAMP) levels were examined in mouse brain. Cyclic GMP levels were dose dependently increased by excitatory drugs such as picrotoxin, pentetrazol, oxotremorine and harmaline in mouse cerebellum and medial forebrain (parts of the cortex, hippocampus, hypothalamus, thalamus, striatum and midbrain) in vivo. Cyclic AMP levels remained unchanged under these conditions. The effects of pretreatment with diazepam, pentobarbital, and atropine on the actions of these drugs are reported. It is concluded that, since pentobarbital and diazepam also decreased cyclic GMP levels in a dose dependent manner in brains of control animals, the changes in cyclic GMP levels observed after administration of excitatory drugs are related to the arousal reaction of the central nervous system. 27 references. (Author abstract modified)

241247 Westfall, Thomas C.; Besson, Marie-Jo; Giorguieff, Marie-Francoise; Glowinski, Jacques. Dept. of Pharmacology, Univ. of Virginia School of Medicine, Charlottesville, VA **The role of presynaptic receptors in the release and synthesis of 3H-dopamine by slices of rat striatum.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 292(3):279-287, 1976.

The role of presynaptic receptors in the release and synthesis of 3H-dopamine (3H-DA) by slices of rat striatum was examined. Potassium induced a marked increase in 3H-DA release and a biphasic effect on synthesis. Benztropine increased the K+ induced overflow of 3H-DA, but failed to alter the inhibition of synthesis. Fluphenazine potentiated 3H-DA release and prevented the inhibition of synthesis both in the absence or presence of benztropine. Exogenous DA increased 3H-DA outflow and reduced DA synthesis, while isoproterenol was without effect. The DA inhibitory effect on synthesis was still observed in the presence of benztropine, while the noradrenaline (NA) effect was prevented. Benz-

tropine blocked both DA and NA uptake. Fluphenazine significantly prevented the decrease in 3H-DA synthesis induced by exogenous DA and partially prevented the effect of NA. Exogenous DA still inhibited the synthesis of DA in the presence of 2-amino-4-hydroxy-6,7-dimethyl-5,6,7,8-tetrahydropteridine hydrochloride. Results support the concept that activation of presynaptic DA receptors located on DA terminals in the striatum of the rat results in an inhibition of synthesis and release of the transmitter. 20 references. (Author abstract modified)

241248 Miller, R. J.; Hiley, C. R. Wellcome Research Lab., 3030 Cornwallis Road, Research Triangle Park, NC 27709 **Anti-dopaminergic and anti-muscarinic effects of dibenzodiazepines: relationship to drug induced parkinsonism.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 292(3):289-293, 1976.

The relationship to drug induced parkinsonism of the antidopaminergic and antimuscarinic effects of dibenzodiazepines was explored. The antidopaminergic effects of several dibenzodiazepines were examined on the dopamine stimulated adenylate cyclase in rat striatal homogenates. The "cis" isomer of clozapine (HF-2046), was the most potent in this respect and perlapine, which is devoid of neuroleptic activity, was the weakest. The antimuscarinic effects of the same compounds were measured by using the muscarinic affinity label 3H-propylbenzylcholine mustard. HF-2046 was the most potent and loxepine the least potent of the drugs used. The antidopaminergic effects of the drugs correlate well with neuroleptic but not with extrapyramidal effects. The antidopaminergic/antimuscarinic ratio, however, correlates well with extrapyramidal rather than neuroleptic effects. 14 references. (Author abstract)

241252 Racagni, G.; Cheney, D. L.; Trabucchi, M.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **In vivo actions of clozapine and haloperidol on the turnover rate of acetylcholine in rat striatum.** Journal of Pharmacology and Experimental Therapeutics. 196(2):323-332, 1976.

Acetylcholine (ACh) content and turnover rate (TR) was measured in striatum and cortex of rats receiving haloperidol and clozapine intraperitoneally. Both clozapine and haloperidol reversed the decrease in striatal TR elicited by apomorphine, while each antipsychotic affected the steady state and the TR in striatum differently. Haloperidol failed to change striatal ACh content but increased the TR; clozapine failed to change striatal ACh content but increased the TR; clozapine neither decreased the content of ACh nor changed the TR in striatum. Clozapine, but not haloperidol, antagonized the increase in ACh content and the decrease in TR elicited by arecoline and oxotremorine in striatum. Clozapine resembled trihexylphenidyl and benztropine because it decreased the ACh content of striatum without changing the TR. Moreover, clozapine and benztropine reversed the increase in striatal TR elicited by haloperidol. The increase in striatal TR elicited by haloperidol could be of value to explain the extrapyramidal action of this drug. It is suggested that the anticholinergic action of clozapine could explain the absence of extrapyramidal side-effects observed with this drug. 47 references. (Author abstract modified)

241253 Neckers, L. M.; Bertilsson, L.; Koslow, S. H.; Meek, J. L. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, WAW Building, Washington, DC 20032 **Reduction of tryptophan hydroxylase activity and 5-hydroxytryptamine concentration in certain rat brain nuclei after p-chloroamphetamine.** Journal of Pharmacology and Experimental Therapeutics. 196(2):333-338, 1976.

High pressure liquid chromatography and mass fragmentography were used to determine tryptophan hydroxylase activity and 5-hydroxytryptamine (5-HT) concentration, respectively, in certain rat brain nuclei. Chloroamphetamine decreased enzyme activity in 5-HT content reamined maximally depleted in septum, the enzyme activity and 5-HT content remained maximally depleted for as long as 2 months after the p-chloroamphetamine injection. Of the 5-HT cell body areas investigated, only in the B9 nucleus was the tryptophan hydroxylase activity and 5-HT content still significantly reduced at 21 and 60 days after the drug injection. The enzyme activity and 5-HT content of the B7 and B8 nuclei were not significantly different from control values at these times. These results suggest that the primary site of action of p-chloroamphetamine is on nerve terminals followed by secondary effects on serotonergic cell bodies. 27 references. (Author abstract)

241254 Friedman, Eitan; Hanin, Israel; Gershon, Samuel. Dept. of Psychiatry, NYU Medical Center, 550 First Avenue, New York, NY 10016 **Effect of tetrahydrocannabinols on 3H-acetylcholine biosynthesis in various rat brain slices.** Journal of Pharmacology and Experimental Therapeutics. 196(2):339-345, 1976.

The effects of delta8-tetrahydrocannabinol and delta9-tetrahydrocannabinol on the biosynthesis of 3H-acetylcholine (ACh) from 3H-choline in cortical, hypothalamic and striatal rat brain slices were examined. The two cannabinols were found to inhibit the synthesis of 3H-ACh in the three brain regions. Treatment with cannabidiol did not alter ACh synthesis. Delta8-tetrahydrocannabinol was approximately twice as effective as the delta9-isomer. This effect was not associated with alterations in striatal and cortical choline acetyltransferase or with an impaired high affinity uptake system for choline in the striatum. Antagonism of the ACh biosynthesis inhibition occurred when slices from treated animals were incubated in depolarizing concentrations of potassium (K+) ion. These results suggest that the inhibition of ACh synthesis observed in tetrahydrocannabinol treated rats may be related to interference with the propagated action potential or with the depolarization process in cholinergic neurons. 38 references. (Author abstract modified)

241255 Komiskey, H. L.; Rudy, T. A. School of Pharmacy, University of Wisconsin, Madison, WI 53706 **The involvement of methysergid-sensitive receptors and prostaglandins in the hyperthermia evoked by 5-HT in the cat.** Research Communications in Chemical Pathology and Pharmacology. 11(2):195-208, 1975.

In a study of methysergid sensitive receptors in the cat, an injection of 5-hydroxytryptamine (5-HT) into the rostral hypothalamus produced an immediate, short-term increase or decrease in body temperature. A delayed and long-term hyperthermia often followed the initial response. When indomethacine was administered intraperitoneally 3 hours prior to an injection of 5-HT at sites which produced an initial increase in body temperature, the secondary hyperthermia was reduced or abolished, but the immediate response remained undiminished. Pretreatment with methysergid attenuated or abolished the initial temperature increase but did not reduce the delayed hyperthermia. The results suggest that the initial rise in body temperature produced by 5-HT is mediated by activation of methysergid sensitive 5-HT receptors and that the response is independent of prostaglandin release. The seconda-

ry hyperthermia, on the other hand, is apparently mediated by a sustained release of prostaglandins. 19 references. (Author abstract)

241256 Teale, J. D.; Clough, Jacqueline M.; Piall, Evelyn M.; King, L. J.; Marks, V. Department of Biochemistry, University of Surrey, Guildford GU2 5XH, England **Plasma cannabinoids measured by radioimmunoassay in rabbits after intravenous injection of tetrahydrocannabinol, 11-hydroxytetrahydrocannabinol, cannabinol, and cannabidiol.** Research Communications in Chemical Pathology and Pharmacology. 11(2):339-342, 1975.

An antiserum raised in sheep against a conjugate of tetrahydrocannabinol with bovine serum albumin was used as the basis of a radioimmunoassay for cannabinoids in the blood of rabbits given tetrahydrocannabinol, 11-hydroxytetrahydrocannabinol, cannabinol or cannabidiol by rapid intravenous injection. In the case of both 11-hydroxytetrahydrocannabinol and cannabinol, plasma cannabinoid concentrations fell exponentially from an initial peak plasma level attained immediately after the completion of intravascular distribution of the injected bolus. In the case of tetrahydrocannabinol itself, however, there was a progressive rise in plasma cannabinoid concentration between 5 and 15 minutes after the rapid intravenous injection. The reasons for this rise in plasma cannabinoid concentration are discussed. 6 references. (Author abstract)

241257 Riffee, W. H.; Gerald, M. C. Division of Pharmacology, College of Pharmacy, Ohio State University, Columbus, OH 43210 **Determinations of endogenous concentrations of norepinephrine and dopamine and their rates of synthesis in a single mouse brain: biphasic effects of (+)-amphetamine.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 219(1):70-78, 1976.

A method is described that possesses sufficient sensitivity to permit the simultaneous fluorometric assay of endogenous concentrations of tyrosine, dopamine and norepinehphrine, and the measurement of the estimated rate of synthesis of 3H-dopamine and 3H-norepinephrine from 3H-tyrosine in a single mouse brain. (+)-Amphetamine elicited a biphasic effect reducing the estimated rate of synthesis of dopamine and norepinephrine at 5mg/kg, while lowering the endogenous concentrations of these catecholamines and increasing their rates of synthesis at 15mg/kg. 33 references. (Author abstract)

241295 Walters, Judith R.; Roth, Robert H. Laboratory of Neuropharmacology, NINCDS, NIH, Bethesda, MD 20014 **Dopaminergic neurons -- alteration in the sensitivity of tyrosine hydroxylase to inhibition by endogenous dopamine after cessation of impulse flow.** Biochemical Pharmacology (Oxford). 25(6):649-654, 1976.

The inhibition of firing in the nigrostriatal dopamine system which causes a rapid increase in the steady state levels of dopamine and an apparent activation in vivo of tyrosine hydroxylase was examined in rat brain. Although the apparent activity of tyrosine hydroxylase returns to normal after dopamine levels have been increased, the elevated dopamine levels do not appear to inhibit tyrosine hydroxylase below control levels. In contrast, when dopamine levels are increased by administration of a monoamine oxidase inhibitor, there is a significant reduction in striatal tyrosine hydroxylase activity as measured by the accumulation of dihydroxyphenylalanine (DOPA) after administration of a DOPA decarboxylase inhibitor. These results suggest that a blockade of impulse flow in the dopaminergic neurons causes a decrease in the sensitivity of striatal tyrosine hydroxylase to inhibition by elevated levels of dopamine. Administration of dopamine agonists reverses this effect and restores to normal the sensitivity of tyrosine hydroxylase to inhibition by endogenous dopamine. Thus, the dopamine agonists appear to alter dopamine synthesis in the absence of impulse flow by interacting at a site, possibly on the presynaptic side of the dopamine terminal. 53 references. (Author abstract modified)

241296 Morgenroth, Victor H., III; Walters, Judith R.; Roth, Robert H. Department of Psychiatry, Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06510 **Dopaminergic neurons -- alteration in the kinetic properties of tyrosine hydroxylase after cessation of impulse flow.** Biochemical Pharmacology (Oxford). 25(6):655-661, 1976.

Alteration in the kinetic properties of tyrosine hydroxylase after cessation of impulse flow was reported in rat brain. Inhibition of impulse flow in the nigrostriatal pathway by either pharmacological or mechanical techniques causes the isolated striatal tyrosine hydroxylase to behave kinetically like the enzyme treated in vitro with calcium chelating agents. Tyrosine hydroxylase, isolated from the striatum of rats in which impulse flow has been interrupted in the dopamine pathways, has an increased affinity for both substrate and pterin cofactor and a reduced affinity for the end product inhibitor, dopamine. These alterations in the kinetic properties of tyrosine hydroxylase can also be completely reversed by addition of calcium to the incubation medium. In rats with a pharmacological blockade of impulse flow induced by administration of gamma-hydroxybutyrate, subsequent administration of dopamine receptor stimulants causes the isolated tyrosine hydroxylase to have properties similar to those observed for the enzyme prepared from untreated rats. 33 references. (Author abstract modified)

241297 Adachi, Yukihiko; Yamamoto, Toshio. Department of Internal Medicine, Kinki University School of Medicine, Sayama-cho, Osaka 589, Japan **Influence of drugs and chemicals upon hepatic enzymes and proteins -- I. Structure-activity relationship between various barbiturates and microsomal enzyme induction in rat liver.** Biochemical Pharmacology (Oxford). 25(6):663-668, 1976.

The effects of phenobarbital, three N-phenylbarbiturates and three N-cyclohexylbarbiturates on microsomal protein content cytochrome P-450, cytochrome b5, aniline hydroxylase, aminopyrine demethylase, p-nitrophenol-glucuronyltransferase and the ultrastructure of hepatic cells in rat liver were studied. Smooth endoplasmic reticulum increased after the administration of phenobarbital, phetharbital or bucolome. Phenobarbital and phetharbital induced cytochrome P-450 and glucuronyltransferase. It is concluded that the type and spatial position of barbiturate substituents are important for hepatic microsomal induction. Data also indicate that the serum bilirubin reducing mechanism of bucolome is different from that of phenobarbital and phetharbital. 28 references. (Author abstract modified)

241298 Nixon, Ralph A. Department of Neuropathology, Harvard Medical School, Boston, MA 02115 **Neurotoxicity of a non-metabolizable amino acid, 1-aminocyclopentane-1-carboxylic acid (ACPC): ACPC transport mechanisms in tissues.** Biochemical Pharmacology (Oxford). 25(6):726-729, 1976.

The neurotoxicity of 1-aminocyclopentane-1-carboxylic acid (ACPC) which is a nonmetabolizable amino acid was examined in mice. The ACPC distribution ratios in brain and spinal cord were not significantly different from unity. Accumulation

against a concentration gradient occurred in kidney, in spleen to a greater degree and to a much greater degree in pancreas. The distribution ratios for central nevous system tissue, kidney and spleen did not change as a function of plasma ACPC concentration or of time between 4 and 50 days after ACPC administration. The results show that ACPC exhibits properties similar to natural amino acids in vivo. The findings support the idea that the neurotoxicity of natural amino acids in disorders of amino acid metabolism may be partly the result of general biochemical responses to the amino acids in their unmetabolized state. 34 references. (Author abstract modified)

241299 Landsberg, Lewis. Beth, Israel Hospital, 330 Brooklin Ave., Boston, MA 02215 **Extraneuronal uptake and metabolism of (3H)L-norepinephrine by the rat duodenal mucosa.** Biochemical Pharmacology (Oxford). 25(6):729-731, 1976.

Extraneuronal uptake and metabolism of (3H)L-norepinephrine (3H-NE) by the rat duodenal mucosa were reported. Treatment with 6-hydroxydopamine (6-OHDA) increased the accumulation of both (3H)L-dopa and (3H)L-NE. The metabolism of NE and L-dopa was unchanged by pretreatment with 6-OHDA. The results indicate that conjugation of (3H)L-NE is a major pathway in duodenal mucosa just as it is for L-dopa. The data imply that duodenal mucosa possess an important inactivating mechanism for the catechol group. 5 references. (Author abstract modified)

241313 Ilhan, M.; Long, J. P.; Cannon, J. G. University of Hacettepe, Institute of Pharmacology and Toxicology, Ankara, Turkey **Effects of some dopamine analogs and haloperidol on response to stimulation of adrenergic nerves using cat atria in vitro.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 219(2):193-204, 1976.

In a pharmacologic study of sympathetic innervation of the cat heart, dopamine analogs, N,N-dimethyldopamine, apomorphine and 5,6-dihydroxy-2-dimethylaminotetralin (M-7) produced inhibition of positive chronotropic and inotropic responses to transmural stimulation of isolated right atria of cats. Haloperidol antagonized inhibitory effects of dopamine analogs. Also haloperidol increased atrial responses during transmural stimulation. N,N-dimethyldopamine, M-7 and apomorphine did not alter responses to exogenous norepinephrine. Haloperidol did not antagonize the inhibitory effect of clonidine. 26 references. (Author abstract)

241315 Ruch-Monachon, M. A.; Jalfre, M.; Haefely, W. Department of Experimental Medicine, F. Hoffmann-La Roche & Co. Ltd., Basel, Switzerland **Drugs and PGO waves in the lateral geniculate body of the curarized cat: I. PGO wave activity induced by Ro 4-1284 and by p-chlorophenylalanine (PCPA) as a basis for neuropharmacological studies.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 219(2):251-268, 1976.

The ponto-geniculo-occipital (PGO) waves induced by Ro-4-1284, a benzoquinolizine derivative and p-chlorophenylalanine (PCPA) were examined in cats. PGO waves were recorded from both lateral geniculate bodies. The density of PGO waves was inversely correlated with the levels of brain noradrenaline (NA) and 5-hydroxytryptamine (5-HT). At the peak of activity, during the second hr following the injection of Ro-4-1284, the density of PGO/1284 was 630/hr; it slightly declined during the following 5 hr. The highest activity of PGO/PCPA appeared around the 74th hr after the first of two injections of PCPA; it remained constant for 3 hr and thereafter gradually declined. In contrast to the regular appearance of PGO/1284, the PGO/PCPA occurred in highly variable bursts. This difference was probably due to the different levels of NA and 5-HT in the brain. 45 references. (Author abstract modified)

241316 Ruch-Monachon, M. A.; Jalfre, M.; Haefely, W. Department of Experimental Medicine, F. Hoffmann-La Roche & Co. Ltd., Basel, Switzerland **Drugs and PGO waves in the lateral geniculate body of the curarized cat: II. PGO wave activity and brain 5-hydroxytryptamine.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 219(2):269-286, 1976.

Ponto-geniculo-occipital (PGO) waves induced either by the benzoquinolizine derivative, Ro-4-1284 (PGO1284), or by the inhibitor of tryptophan hydroxylase, p-chlorophenylalanine (PGO/PCPA), were continuously recorded and counted in the lateral geniculate bodies of unanesthetized immobilized cats. The density of PGO waves was dose dependently decreased and the waves were eventually abolished by the precursors of 5-hydroxytryptamine (5-HT), L-tryptophan and 5-hydroxytryptophan. 5-HT itself tended to diminish the density. Lysergic acid diethylamide (LSD) was an extremely potent depressor of PGO1284 and PGO/PCPA; psilocybin was almost as potent as LSD, whereas higher doses of N,N-dimethyltryptamine, bufotenine and yohimbine were required for the reduction of PGO waves. A number of tricyclic antidepressants reduced the density of PGO waves, their order of potency corresponding to that reported for their inhibitory effect on the uptake of 5-HT. Two dibenzothiepine antipsychotics, methiothepin and octoclothepin, increased the density of PGO1284 and PGO/PCPA and also induced PGO waves in untreated cats. The evidence suggests that these two compounds antagonize the effect of endogenous 5-HT in the brain. 53 references. (Author abstract modified)

241317 Ruch-Monachon, M. A.; Jalfre, M.; Haefely, W. Department of Experimental Medicine, F. Hoffmann-La Roche & Co. Ltd., Basel, Switzerland **Drugs and PGO waves in the lateral geniculate body of the curarized cat: III. PGO wave activity and brain catecholamines.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 219(2):287-307, 1976.

The possible implication of central catecholamines in the phasic phenomenon of ponto-geniculo-occipital (PGO) waves was investigated in cats using PGO waves induced by the benzoquinolizine derivative, Ro-4-1284 (PGO/1284), and the inhibitor of tryptophan hydroxylase, p-chlorophenylalanine (PGO/PCPA). Injections of noradrenaline (NA) and of dopamine (DA) into the lateral brain ventricle tended to decrease the density of PGO/1284. The stimulant of central alpha-adrenoceptors, clonidine, suppressed PGO/1284 and PGO/PCPA in very small doses. Apomorphine in high doses had inconsistent depressant effects which were probably not related to its stimulant action on DA receptors. Release of brain NA by dexamphetamine and beta-tetrahydronaphthylamine decreased the density of PGO waves. The monoamine oxidase inhibitor, nialamide, depressed PGO/PCPA more than PGO/1284, whereas pheniprazine was inactive. The inhibitor of catechol-O-methyltransferase, tropolone, reduced the density of both PGO/1284 and PGO/PCPA. Desimipramine, which preferentially blocks the uptake of NA, was more potent on PGO/PCPA than on PGO/1284. The alpha-adrenoceptor blocking agent, phenoxybenzamine, markedly increased the density of PGO/PCPA. The results suggest that NA neurons originating in the locus coeruleus depress neurons in the pontine reticular formation involved in the generation of PGO waves. 43 references. (Author abstract modified)

241318 Ruch-Monachon, M. A.; Jalfre, M.; Haefely, W. Department of Experimental Medicine, F. Hoffmann-La Roche & Co. Ltd., Basel, Switzerland **Drugs and PGO waves in the lateral geniculate body of the curarized cat: IV. The effects of acetylcholine, GABA and benzodiazepines on PGO wave activity.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 219(2):308-325, 1976.

The possible involvement of cholinergic mechanisms and of gamma-aminobutyric acid (GABA) in the modulation and generation of ponto-geniculo-occipital (PGO) waves was studied in cats using PGO waves induced by the benzoquinolizine derivative, Ro-4-1284 (PGO/1284), and by p-chlorophenylalanine (PGO/PCPA). Atropine had no significant effect on PGO/1284 but markedly depressed the density of PGO/PCPA; this effect of atropine was absent when the synthesis of noradrenaline (NA) was inhibited in addition to that of 5-hydroxytryptamine (5-HT). GABA injected into a lateral brain ventricle augmented the density of PGO/PCPA but not of PGO/1284. Increasing the level of endogenous GABA by amino oxyacetic acid and by hydroxylamine affected PGO waves like GABA. Bicuculline tended to decrease the density of PGO/PCPA. It is concluded that synapses with nicotinic cholinergic receptors are present either in the neuronal network of the pontine reticular cells which trigger the PGO waves or within the pathway leading from this area to the lateral geniculate body. The pathway originating in the forebrain and projecting to the locus coeruleus seems to be inhibitory for noradrenaline neurons and to contain muscarinic and GABA mediated synapses. 27 references. (Author abstract modified)

241319 Ruch-Monachon, M. A.; Jalfre, M.; Haefely, W. Department of Experimental Medicine, F. Hoffmann-La Roche & Co. Ltd., Basel, Switzerland **Drugs and PGO waves in the lateral geniculate body of the curarized cat: V. Miscellaneous compounds. Synopsis of the role of central neurotransmitters on PGO wave activity.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 219(2):326-346, 1976.

The role of central neurotransmitters on ponto-geniculo-occipital (PGO) waves induced by the benzoquinolizine derivative Ro-4-1284 (PGO/1284) and by p-chlorophenylalanine (PGO/PCPA) were examined. Hypnotic sedatives of different classes had no significant effects in doses that did not markedly alter the electrical background activity of the lateral geniculate bodies. A notable exception was gamma-hydroxybutyric acid which increased the density of PGO/1284 and PGO/PCPA. A number of neuroleptics were found inactive; sulpiride surprisingly decreased the density of PGO/1284. Bulbocapnine had a similar effect. Convulsants in subconvulsive doses did not uniformly affect PGO waves: while pentetrazole had no consistent effect, strychnine decreased and picrotoxin increased the density of PGO/1284. Ethanol was inactive even in high doses. Caffeine and mefexamide reduced the density of PGO/1284. Mepiprazol was the most potent depressant of PGO/1284, probably by inhibiting the uptake of 5-HT. The results suggested a tentative scheme of the generation and modulation of PGO waves, in which the hypothetical roles and sites of action of four central neurotransmitters are included. 60 references. (Author abstract)

241328 Gilden, Lloyd; Kozakiewicz, Raymond. Dept. of Psychology, Queens College, Flushing, NY 11367 **The effect of morphine on the EEG of the hypothalamus in the rat.** Physiology & Behavior. 16(2):169-176, 1976.

Electrographic changes occurring in the hypothalamus rats after saline, 8mg/kg or 16mg/kg intraperitoneal injections of morphine were recorded. The data were subjected to spectral analysis, and statistical comparisons were made of changes in intensity and percent of total intensity occurring in each of the standard frequency bands under the various conditions. The effects varied for different electrode sites, but a general trend toward increases in both intensity and percent of theta and alpha activity and decreases in delta activity with the drug was observed. Frequent occurrence of spike/dome activity was also noted. The possible relationship between spectral analysis profiles, spike/dome discharges and unit activity are discussed, and consideration is given to the possibility that a shift toward high amplitude, synchronous electrical activity in the hypothalamus is a correlate of the positive reinforcing effects of morphine. 25 references. (Author abstract modified)

241338 Ho, Ing K.; Yamamoto, Ikuo; Loh, Horace H.; Way, E. Leong. Dept. of Pharmacology, University of Mississippi Medical Center, Jackson, MS 39216 **Effects of chronic administration of morphine on pentobarbital responses in the mouse.** Biochemical Pharmacology (Oxford). 25(3):357-358, 1976.

Evidence that morphine can inhibit drug microsomal activity in both male and female mice is presented. The chronic administration of morphine by 3 days of pellet implantation potentiated the effects of pentobarbital on sleeping time and on lethality in both male and female mice. The toxicity of pentobarbital in the morphine pellet implanted male or female mice was also increased. The ability of hepatic microsomal enzyme to metabolize ethylmorphine in male and female mice was the same. Morphine had a significant inhibitory effect on microsomal metabolism of ethylmorphine in both sexes. It is suggested that the enhancement of the prolongation in pentobarbital sleeping time by chronic morphine administration of morphine can be attributed to a large extent to inhibition of drug microsomal activity. This indicates that chronic administration of morphine can enhance the responses to pentobarbital, and decrease the metabolism of ethylmorphine in mice. 16 references.

241339 Fuller, Ray W.; Perry, Kenneth W. Lilly Research Laboratories, Eli Lilly & Co., Indianapolis, IN 46206 **Inability of methadone to prevent the depletion of brain 5-hydroxyindoles by p-chloroamphetamine.** Biochemical Pharmacology (Oxford). 25(3):360-361, 1976.

The inability of methadone to prevent the depletion of brain 5-hydroxyindoles by p-chloroamphetamine in rats is reported. The depletion of brain serotonin and 5-hydroxyindoleacetic acid (5-HIAA) by p-chloroamphetamine in rats is also reported. The depletion of brain serotonin and 5-hydroxyindoleacetic acid (5-HIAA) by p-chloroamphetamine (PCA) was not altered significantly by l-methadone. Lilly-110140, a known inhibitor of serotonin uptake, completely antagonized the depletion of serotonin by PCA. The failure of methadone alone to lower 5-HIAA levels indicates that it does not inhibit serotonin uptake. Neither isomer of methadone nor dl-methadone had any effect on 5-HIAA levels in mouse brain. The results suggest that inhibition of serotonin reuptake does not play a part in the pharmacological effects of methadone. 26 references.

241343 Chakrabarty, Indira; Sengupta, D.; Bhattacharya, P.; Ghosh, J. J. Department of Biochemistry, University College of Science, 35, Ballygunge Circular Road, Calcutta-19, India **Effect of cannabis extract on the uterine monoamine oxidase activity of normal and estradiol treated rats.** Biochemical Pharmacology (Oxford). 25(4):277-278, 1976.

The effects of repeated administration of cannabis extract on monoamine oxidase (MAO) activity of uterine tissues of prepuberal rats, treated with or without estradiol benzoate at two time intervals, were studied. Results indicate that the MAO activity of uterine tissues is increased significantly by cannabis extract both in normal as well as in estradiol treated rats. Estradiol, on the other hand, decreased the enzyme activity significantly by itself. The increase in MAO activity following cannabis extract administration is more prominent in 14 hr than in the 40 hr hormone treated groups. 17 reference.s(Author abstract)

241344 Procaccini, Robert L.; Mathur, Pershotam P.; Smyth, Robert D.; Reavey-Cantwell, Nelson H. Rorer Research Laboratories, Fort Washington, PA 19034 **Comparative effect of phenobarbital and methaqualone on warfarin metabolism in the rat.** Biochemical Pharmacology (Oxford). 25(4):379-382, 1976.

The effect of methaqualone or phenobarbital pretreatment on the metabolism of (14C)warfarin in the rat was studied in order to ascertain to what extent phenobarbital and methaqualone, a nonbarbiturate sedative hypnotic, affect the pattern of warfarin metabolism. A decrease in the plasma concentration of warfarin was observed 5-24 hr after administration of (14C)warfarin to phenobarbital pretreated animals. Methaqualone pretreatment did not significantly affect the plasma concentration of intact warfarin. Significantly higher levels of metabolites were found in the plasma of phenobarbital pretreated animals as compared to either methaqualone treated or control groups. These data indicate a marked difference in the ability of phenobarbital and methaqualone to alter warfarin metabolism, even though both drugs have been shown to induce hepatic drug metabolism. 23 references. (Author abstract)

241345 Holmes, John C.; Rutledge, Charles O. Department of Pharmacology, University of Colorado, School of Medicine, Denver, CO 80220 **Effects of the d- and l-isomers of amphetamine on uptake, release and catabolism of norepinephrine, dopamine and 5-hydroxytryptamine in several regions of rat brain.** Biochemical Pharmacology (Oxford). 25(4):447-451, 1976.

The stereoselectivity of d-amphetamine and l-amphetamine for uptake, release and catabolism of biogenic amines was studied in vitro in three regions of rat brain. The d-isomer was about two times more potent than the l-isomer in inhibiting uptake and releasing biogenic amines from chopped cerebral cortex labeled with norepinephrine and midbrain labeled with 5-hydroxytryptamine. On the other hand, the d-isomer was five times more potent than the l-isomer in inhibiting the uptake and releasing (3H)dopamine from nerve terminals of corpus striatum. When the relative potencies of amphetamine on uptake and release were compared, it was found that approximately 11 fold higher concentrations of both isomers were required to release dopamine compared to their ability to inhibit neuronal uptake. Only four fold higher concentrations of both isomers of amphetamine were required to release (3H)norepinephrine compared to their ability to inhibit neuronal uptake. These results indicate that the dopamine nerve terminals of the corpus striatum possess greater stereoselectivity toward amphetamine than either the norepinephrine nerve terminals of cerebral cortex or 5-hydroxytryptamine neurons of midbrain. 41 references. (Author abstract modified)

241346 Mycek, Mary J.; Brezenoff, Henry E. Dept. of Pharmacology, College of Medicine and Dentistry, New Jersey Medical School, Newark, NJ 07130 **Tolerance to centrally administered phenobarbital.** Biochemical Pharmacology (Oxford). 25(5):501-504, 1976.

In a study of tolerance to centrally administered phenobarbital, rats with permanent indwelling cerebral ventricular cannulae were shown to lose their righting reflex. Administration of four daily injections of phenobarbital over a 4 to 5 day period produced a gradual tolerance to the hypnotic effect, which was reversible after suspension of the drug regimen. This tolerance was associated with an increase in hepatic drug metabolizing activity, measured as p-nitroanisole demethylase. The microsomal enzymes were excluded as mediators of tolerance, however, on the basis of temporal and quantitative comparisons between the level of hepatic enzymatic activity and the degree of tolerance. The data are consistent with the concept that tolerance to the hypnotic action of phenobarbital is mediated through an adaptation of the central nervous system. 15 references. (Author abstract modified)

241347 Miller, Richard J. MRC Neurochemical Pharmacology Unit, Dept. of Pharmacology, Medical School, Hills Rd., Cambridge CB2 2QD, England **Comparison of the inhibitory effects of neuroleptic drugs on adenylate cyclase in rat tissues stimulated by dopamine, noradrenaline and glucagon.** Biochemical Pharmacology (Oxford). 25(5):537-541, 1976.

The effect of neuroleptic drugs of various chemical classes on adenylate cyclase from a variety of rat tissues was investigated. These were the dopamine stimulated adenylate cyclase in rat striatal homogenates, the noradrenaline stimulated adenylate cyclase in adipocyte membrane fragments and the glucagon stimulated adenylate cyclase in liver membranes. Stimulation could be rapidly inhibited by several classes of neuroleptic agents. The inhibitory effect of neuroleptics of all classes was completely reversed by high concentrations of dopamine, and this reversal took place rapidly at 30 degrees centigrade. Neuroleptics were also able to inhibit the stimulatory effects of noradrenaline on adipocyte adenylate cyclase at concentrations where the basal enzyme activity was not affected. The potencies of drugs as inhibitors in this system again did not correlate with neuroleptic potencies. Higher concentrations of glucagon were not able to reverse the inhibition produced by neuroleptics. It is concluded that the effects of neuroleptic drugs on dopamine stimulated adenylate cyclase correlate most closely with their clinical neuroleptic potencies. 25 references. (Author abstract modified)

241348 Roth-Schechter, Barbara F.; Mandel, Paul. Centre de Neurochimie du CNRS, 11 Rue Humann, 67085 Strasbourg Cedex, France **A study on the development of barbiturate tolerance and dependence in hamster glial cells in culture.** Biochemical Pharmacology (Oxford). 25(5):563-571, 1976.

The development of barbiturate tolerance and dependence in hamster glial cells in culture was examined. Profound morphological changes were induced in a dose/time related fashion by pentobarbital only. These consisted of growing of cellular expansions, parallel cellular arrangement, and increased amounts of intracellular material. Exposure of the cells to morphine for up to 6 weeks results in a dose correlated decreased rate of proliferation, but no specific morphological alteration could be observed. The morphological changes induced in cultured glial cells by pentobarbital were accompanied by an increase in oxygen consumption as well as an increase in glucose uptake. These effects were compared to those obtained with bromodeoxyuridine which affected glucose metabolism similarly. Furthermore, glial cells that had been treated for 4 weeks with the barbiturate were less sensi-

tive to the depression of oxygen consumption by a challenging dose of pentobarbital sodium, signifying the development of cellular tolerance. After culturing the cells in barbiturate for 4, 9 or 14 weeks, normal medium was substituted. This resulted in severe degenerative changes and cell deaths as well as altered growth characteristics in the surviving cells, demonstrating some degree of cellular dependence on the barbiturate. 18 references. (Author abstract modified)

241360 Nagatsu, Toshiharu. Dept. of Biochemistry, School of Dentistry, Aichi-Gakuin University, Nagoya 464, Japan **Symposium II. Pharmacology on brain monoamines: 1) abnormality in central noradrenergic neurons in spontaneously hypertensive rats.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):10P-11P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, abnormality in central noradrenergic neurons in spontaneously hypertensive (SH) rats was reported. The activity of dopamine-beta-hydroxylase (DBH) in serum, which is mainly released from the peripheral sympathetically innervated organs, was found to be elevated only when SH rats were very young, as compared with that of normotensive Wistar-Kyoto rats which decreased during the development of hypertension to a level similar to that of normotensive Wistar-Kyoto rats. In the brains of SH rats and control Wistar-Kyoto rats at 3 weeks old DBH activities were found only in the regions of noradrenergic neurons, such as locus coeruleus and hypothalamus, and were very low in the dopaminergic regions such as substantia nigra and caudate nucleus. The noradrenergic neurons in the brainstem are assumed to act for the depression of the peripheral sympathetic nerves through an alpha receptor to decrease the blood pressure, whereas those in the hypothalamus are assumed to act for the activation of the peripheral sympathetic nerves through a beta-receptor to increase the blood pressure. Both the decreased DBH levels in the locus coeruleus and the increased tyrosine hydroxylase levels in the hypothalamus may contribute to the increased peripheral sympathetic nerve activity which was proved in young SH rats. (Author abstract modified)

241361 Segawa, Tomio; Nomura, Yasuyuki; Tanaka, Akiyoshi; Saito, Kazuko. Department of Pharmacology, Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine, Hiroshima 734, Japan **Symposium II. Pharmacology on brain monoamines: 2) neurochemical standpoint.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):11P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of mitotic toxins and antidepressants on the uptake of 5-hydroxytryptamine (5-HT) as well as norepinephrine (NE) into synaptosomes and small vesicles from rat brain were reported. Uptake of 5-HT and NE into synaptosomes was significantly inhibited by ouabain, colchicine (CH) and vinblastine (VB). The mitotic toxins did not inhibit the uptake of either amine into small vesicles, but when cytoplasmic supernatant was present, VB showed a significant inhibition of the uptake of both amines into this fraction and there was a certain tendency for the uptake of both amines to be decreased by CH. It is suggested that a factor which participates in inhibitory action of the mitotic toxins and has Mg-ATPase and Ca-ATPase activity is present in the cytoplasmic supernatant fraction. The antidepressants which selectively inhibit the NE uptake into synaptosomes antagonize tetrabenazine induced decrease in spontaneous motor activity of mice. In contrast, agents which selectively inhibit the uptake of 5-HT decrease spontaneous motor activity in tetrabenazine treated mice. It is suggested that central 5-HT neurons play a role in decreasing spontaneous motor activity of mice while NE neurons participate in increasing this activity. (Author abstract modified)

241365 Ozaki, Masayori; Sugawara, Kazunobu; Takami, Naoko. 2nd Department of Pharmacology, Nagasaki University School of Medicine, Nagasaki 852, Japan **Effect of 6-hydroxydopamine on the neonate spontaneously hypertensive rat and normotensive rat.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):19P-20P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the nature of the strain difference between the normotensive Wistar rat (NR) and spontaneously hypertensive rat (SHR) was reported. 6-Hydroxydopamine (6-OHDA) was used to chemically sympathectomize the newborn of NR and SHR. In the NR, the growth rate, the blood pressure and the contents of norepinephrine (NE) of the heart and brain cortex were all significantly lower than the controls during the 4 month period. In the SHR, there were no significant changes in the growth rate between controls during the 4 months. The NE of the cortex was lower than controls for the 4 month period, whereas the NE of the medulla was lower than controls after the third month. In comparing the effect of 6-OHDA sympathectomy on the SHR with that of the NR, the growth rate of the NR was affected to a greater extent than the SHR and the mortality of NR was greater than in the SHR after the treatment period. The blood pressure of NR was reduced for a longer duration than that of the SHR and the NE contents of the heart of the NR were affected for a longer period than that of the SHR. These results indicate that the sympathetic nervous system of SHR is more resistant than that of NR. (Author abstract modified)

241366 Nomura, Yasuyuki; Naitoh, Fumiko; Segawa, Tomio. Department of Pharmacology, Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine, Hiroshima 734, Japan **Spontaneous and guanethidine-induced changes of regional monoamine content and monoamine uptake during postnatal development of the rat brain.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):27P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, regional norepinephrine (NE), dopamine (DA) and serotonin (5-hydroxytryptamine, 5-HT) contents in the developing rat brain were reported. The rate of increase in NE content was the highest in the diencephalon and DA concentration revealed marked increase in limbic striatum. In each region, 5-HT content increased gradually but the rate of increase in the diencephalon was relatively high. The results suggest that with increasing age, projections of both NE and 5-HT neurons were relatively high into limbic striatum and hypothalamus and those of the DA neuron were concentrated in the striatum. Guanethidine induced decrease of NE content in limbic striatum at day 7, day 30 and a significant increase in the lower brainstem at day 30. DA content in limbic striatum and in neocortex at day 7, 14, 30 showed a decrease with guanethidine treatment. It was suggested that guanethidine, being able to penetrate the blood/brain barrier during the neonatal period, induces a degeneration of terminals and collateral accumulation in the central NE and DA neurons. (Author abstract modified)

241369 Nakamura, Keiji; Nakamura, Kazuo. Nippon Roche Research Center, Kamakura 247, Japan **Changes in brainstem monoamine neurons after surgical and chemical denervation of the olfactory bulb (OB) in rats.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):46P-47P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, changes in brainstem monoamine neurons after denervation of the olfactory bulb (OB) in rats were reported. Bilateral OB ablation increased content in the brainstem, and there was an elevation of norepinephrine (NE) turnover in the brainstem measured by tyrosine hydroxylase inhibition. The ablation had no effect on most of dopamine neurons except for a decrease in DA turnover in the cortex. The OB ablation significantly decreased 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) contents in the brainstem and hypothalamus. The 6-hydroxydopamine treatment markedly exerted persistent aggressive behavior after a latent period of 10 days, whereas 5,6-dihydroxytryptamine had no influence on the behavior but did significantly decrease 5-HIAA contents in the pons medulla and hypothalamus. These results suggest that aggressive behavior induced by the bilateral OB ablation may have a causal relation to the enhanced NE turnover at the brainstem but not to the decreased 5-HT turnover. The results of a reciprocal change in hindbrain NE and 5-HT cell bodies following denervation of both peripheral nerve terminals at the OB granule cell area may indicate that functions of NE and 5-HT cell bodies are under the control of respective nerve terminals. (Author abstract modified)

241381 Itoh, Tadanobu; Koseki, Yoshihiro; Ando, Fusae; Nakaya, Shigetsuna. Department of Pharmacology, Iwate Medical University, School of Medicine, Morioka 020, Japan **Effects of long-term administration of levomethiomeprazine to rats.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):55P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, levomethiomeprazine (LM) induced symptoms and effects of LM on the blood and tissues of mice and rats were reported. Inhibition of motility, lethargy, drop of rectal temperature and slight paroxysmal clonic convulsion were observed after 5 to 10 min of every administration of LM and such effects lasted for a few days, but about 10 days later the degree of these symptoms decreased and the duration shortened. The average amount of water and food ingested per rat per day was less in the animal group on LM. Weights of bodies and organs increased with administration of LM, but decreased with more than 60mg/kg. Histological examination revealed decomposition and degeneration of epithelial cells at the straight tubuli in the kidney, fatty degeneration of hepatic cells at the peripheral lobuli in the liver, swelling of nervous cells in the brain, degeneration of epithelial cells, decrease in colloidal amounts in the thyroid, and increase in the number of megakaryocytes in the bone marrow. (Author abstract modified)

241383 Ito, Tsugutaka; Yoshida, Kouichi; Shimizu, Masanao. Research Laboratories, Dainippon Pharmaceutical Co. Ltd., Suita, Osaka 564, Japan **Effect of 1,2-benzisoxazole-3-acetamidoxime on caudato-thalamo-cortical system in cats.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):71P-72P, 1975,

At the 48th general meeting of the Japanese Pharmacological Society, the effect of 1,2-benzisoxazole-3-acetamidoxime hydrochloride (PF-257) on the caudate spindle was reported. PF-257 changed the spontaneous electroencephalogram (EEG) arousal patterns to drowsy ones. A high dose of the compound accelerated the arousal patterns. PF-257 showed little or no effect on the EEG arousal response induced by stimulating the sciatic nerve. On the other hand, a high dose of the compound facilitated the response. PF-257 at 5 and 10mg/kg depressed the caudate spindle elicited by stimulating the head of the caudate nucleus. The compound at 10mg/kg enhanced the caudate spindle after an initial depression in the response. PF-257 facilitated both recruiting response and cortical focal seizure elicited by stimulating the thalamus and the visual cortex, respectively. A high dose of the compound reduced the recruiting response after an initial increase in the response. It would appear that PF-257 acts selectively on the caudate nucleus involved in the dopaminergic system and that the depression of this nucleus by the compound probably results in an increase in susceptibility of the thalamo/cortical region. (Author abstract modified)

241384 Ito, Keizo; Nurimoto, Seiichi; Kudo, Yukitsuka; Ishida, Ryuichi. Safety Research Laboratory, Tanabe Seiyaku Co. Ltd., Osaka 532, Japan **Neuropharmacological effects of penfluridol, a new antipsychotic agent.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):74P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the neuropharmacologial effects of penfluridol (TLP-607) were compared with those after haloperidol and chlorpromazine. Acute oral and intraperitoneal toxicities of TLP-607 were approximately equal to haloperidol and chlorpromazine in mice. Spontaneous motor activity of mice was significantly suppressed by TLP-607. Like haloperidol and chlorpromazine, TLP-607 induced catalepsy lasting for 48-72 hr. This activity was 0.2and 2.2times as potent as that of haloperidol and chlorpromazine respectively. TLP-607 strongly inhibited apomorphine induced emesis in dogs. TLP-607 suppressed methamphetamine induced stereotyped behavior in rats. TLP-607 also inhibited conditioned avoidance responses in rats and the ED50's in pole climbing and Sidman avoidance methods were 6.7and 3.4mg/kg p.o. respectively. Hyperemotionality of the rats with olfactory bulb ablations was slightly suppressed by TLP-607. It is concluded that TLP-607 is a potent and long-acting antipsychotic drug with few neurotoxic side-effects. (Author abstract modified)

241385 Ikeda, Shigeru; Murayama, Satoshi. Development Department, Kissei Pharmaceutical Co. Ltd., Matsumoto 399-65, Japan **Effects of perimetazine and chlorpromazine on the transcallosal response in rabbits.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):74P-75P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the action of perimetazine on the transcallosal response in rabbits, was compared with the effects of other central acting drugs. Physostigmine or L-dopa decreased the amplitude of transcallosal potential 30 to 60 min after the administration. The response was not affected by electrical stimulation of the midbrain reticular formation which induced electroencephalogram desynchronization. Perimetazine chlorpromazine or pentobarbital enhanced the amplitude of the potential. On the other hand, a large dose of 5mg/kg of chlorpromazine rather suppressed the amplitude and this suppression was restored with a small dose of pentobarbital. The depression induced by physostigmine was affected by atropine or pentobarbital but was not changed by either perimetazine or chlorpromazine. These results suggest that a cholinergic mechanism may play a role in the transcallosal response and that major tranquillizers (phenothiazines) and general anesthetics (barbiturates) may act in different ways on this mechanism. (Journal abstract modified)

241386 Maruyama, Shoji. Department of Pharmacology, Yamagata University School of Medicine, Yamagata 990-23, Japan **Interaction between possible transmitters and butyrophenones applied microelectrophoretically in the cerebellum and basal ganglia of the cat. 2nd report: effects of some**

phenothiazines on the Purkinje cells of the cerebellum. Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):77P-78P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of some phenothiazines on the Purkinje cell activities of the cat cerebellum were reported. Chlorpromazine and 3-methylsulfonyl-10-2-(1-methyl-2-piperidyl)-ethyl-phenothiazine, one of thioridazine derivatives, produced no inhibitory or excitatory action on the spontaneous firing of Purkinje cells. These drugs did not affect the depressant action of concurrently administered gamma-aminobutyric acid (GABA) on the spontaneous firing of Purkinje cells. Examinations were then made of the effects of glycine and imidazole acetic acid (IAA) on the spontaneous firing of Purkinje cells. Droperidol appeared to enhace the depressant action of glycine in some Purkinje cells and not at all in others. Microelectrophoretically applied bicuculline did not block the depressant action of glycine, but antagonized the inhibitory action of droperidol. IAA also depressed the spontaneous firing of Purkinje cells. This depressant effect of IAA was enhanced by droperidol and blocked by bicuculline, but not affected by chlorpromazine, which did not affect the depressant action of glycine at all. The results suggest that phenothiazine may not produce a GABA like effect at the GABA operated synapses. (Author abstract modified)

241388 Yamamoto, Ken-ichi; Hirose, Katsumi; Naito, Yukio; Yoshizaki, Toshio; Kurosawa, Atsushi; Ogawa, Yasunao; Oka, Motoo. Shionogi Research Lab., Shiongoi & Co., Osaka 533, Japan **Brain function and biogenic amines (4). Role of monoaminergic mechanism on selective inhibition of paradoxical sleep.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):82P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the role of monoaminergic mechanism on selective inhibition of paraadoxical sleep was reported. 1-Methyl-2-(2-naphtyl) aziridine (250059-S) had a potent depleting activity on norepinephrine (NE) in rat brain and heart, and guinea pig vas deferens. The uptake of 14C-NE by guinea pig vas deferens was as strongly inhibited (77%) by 250059-S as by chlorpromazine. The uptake of 14C-NE by bovine adrenal granules was also as inhibited by the compound (79%) as by reserpine. Corresponding to the above biochemical change of brain monoamines, neuroleptic-like behavioral changes such as inhibition of Sidman's avoidance response in rats and monkeys, inhibition of blood pressure rise with NE, antidepressant like effects such as potentiation of amphetamine induced locomotor activities in mice and complete reversal of electroencephalographic reserpine syndrome, and tranquilizer-like effects. The 250059-S induced the selective inhibition of paradoxical (REM) sleep in rats, cats and monkeys; 10mg/kg of the compound induced long-lasting suppression of REM sleep for 48 hr in cats. The lost REM sleep tended to result in an increase of slow wave sleep. Repetitive injection for 2-4 weeks to cats or monkeys caused complete REM sleep deprivation during the period. (Author abstract modified)

241389 Kawasaki, Hiromu; Watanabe, Shigenori; Ueki, Showa. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka 812, Japan **Changes in cardiovascular responses to brain stimulation following olfactory bulbectomy and the effects of psychotropic drugs in rats.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):83P-84P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of bilateral olfactory bulb (OB) lesions on blood pressure (BP), heartrate (HR) and the pressor response to electrical stimulation of the posterior hypothalamus (PH) and midbrain reticular formation (MRF) were reported in freely moving rats. The exploratory behavior was much less in OB rats than in the inact ones. The HR in sham rats was the same as in intact rats, while it was significantly lower in OB rats than in sham rats. The pressor response to MRF stimulation in O.B. rats was markedly augmented on the 5th day after operation. In intact rats, MRF stimulation with 1.77 volts elicited the pressor response of 28mmHg, while the same voltage caused the response of approximately 60mmHg in OB rats on the fifth day after operation. The threshold of behavioral arousal response to MRF stimulation was also lowered in OB rats. The pressor response to PH stimulation was also augmented, though slightly in OB rats on the 10th day after operation. The pressor response to both PH and MRF stimulation was suppressed by diazepam and chlorpromazine, but there were no differences in this effect between OB and sham rats. It is suggested that olfactory bulb lesions cause a marked alteration especially of MRF activity in regulating BP. (Author abstract modified)

241390 Yamamoto, Tsuneyuki; Watanabe, Shigenori; Ueki, Showa. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka 812, Japan **Pharmacological studies on the midbrain raphe system (III). Effects of midbrain raphe stimulation and lesion on EEG activity in rats.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):84P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of electrical stimulation and lesion of medical raphe nuclei (MR) on electroencephalogram (EEG) activity of the frontal cortex, hippocampus, septum and amygdala which were examined in unrestrained Wistar King A rats with chronic electrode implants were reported. After MR stimulation, locomotor activity was reduced and EEG activity changed to a marked drowsy pattern consisting of high voltage slow waves in neocortical EEG and desynchronization of hippocampal EEG. These changes in EEG and behavior were more marked 1 hr after MR stimulation was terminated, and rats appeared to sleep continuously with closed eyes, but an arousal pattern sometimes intervened in EEG; i.e.,dissociation between EEG and behavior was elicited. The EEG drowsy pattern was easily abolished by auditory stimulation. On the other hand, MR lesion elicited significant arousal in EEG and behavior. The change in hippocampal EEG was the most characteristic. When 5-hydroxytryptophan (5-HTP) was administered 10 days after MR lesions, the hippocampal EEG was desynchronized and significantly decreased in voltage, but neocortical EEG was little changed. The results suggest that MR have an important inhibitory influence upon the synchronized EEG activity in the hippocampus. (Author abstract modified)

241391 Watanabe, Hiroshi; Kuno, Hiroshi; Watanabe, Kazuo. Research Institute for Wakanyaku, Toyama University, Toyama 930, Japan **Effects of lowering the serotonin content in the rat brain on gastric ulcer induced by water-immersion stress.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):88P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the incidence of gastric ulcer induced by water immersion stress in male Wistar rats of which brain serotonin was reduced by p-chlorophenylalanine (PCPA), midbrain raphe lesion or 5,6-dihydroxytryptamine (5,6-DHT) was reported. Serontonin content of the forebrain was lowered to less than a level of the unhandled control, although 5-hydroxy-in-

doleacetic acid content was increased as compared with the control level after the stress. When PCPA was given 48 and 24 hr before stress, gastric ulcer was significantly exacerbated. The exacerbation was recovered to the severity of saline control by concomitant administrations of seryl-2,3,4-trihydroxylbenzylhydrazine HCl (Ro 4-4602) and L-5-hydroxytryptophan (5HTP) in PCPA treated rats. Serotonin content of the forebrain was markedly reduced by PCPA and stress, and the reduction was recovered to a level of the saline control after concomitant administrations of Ro 4-4602 and 5HTP. Gastric ulcer induced by stress was slightly suppressed 5 days after an intraventricular injection of 5,6-DHT. The results indicate that water immersion stress increases turnover of serotonin in the forebrain. (Author abstract modified)

241392 Nakanishi Michio; Setoguchi, Michihide. Research Laboratories, Yoshitomi Pharmaceutical Industries Ltd., Fukuoka 871, Japan **Effects of anti-anxiety drugs on cerebral monoamine turnover.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):89P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of diazepam (DZP), chlordiazepoxide (CDP) and clotiazepam (Y-6047), known as antianxiety drugs, on the turnover of cerebral catecholamines (CA) and serotonin (5-HT) which were studied in comparison with antidpressants (imipramine, amitriptyline) and antipsychotic drugs (chlorpromazine, haloperidol) were reported. The rate of disappearance of CA after inhibition of their biosynthesis with alpha-methyl-p-tyrosine and the accumulation of 5-hydroxyindoleacetic acid after probenecid treatment were taken as an index of CA turnover and 5-HT turnover, respectively. In nonstressed rats, the antianxiety drugs were found to decrease 5-HT turnover as well as imipramine and amitriptyline. On the CA turnover, however, they had no effect. Chlorpromazine and haloperidol increased the rate but failed to influence 5-HT turnover. In rats exposed to stress (electrical foot shocks) for 1 hr, the cerebral turnover of CA and 5-HT was found to be accelerated. DZP and Y-6047 significantly depressed the acceleration of CA turnover induced by the stress, while CDP exerted no influence. It is suggested that the antianxiety drugs decrease more potently the turnover of cerebral monoamine (especially the 5-HT) in stressed animals than in nonstressed ones. (Author abstract modified)

241393 Karasawa, Tadahiko; Masuda, Yoshinobu; Furukawa, Kiyoshi; Yoshida, Kouichi; Shimizu, Masanao. Department of Pharmacology, Research Laboratories, Dainippon Pharmaceutical Co. Ltd., Suita, Osaka 564, Japan **Effects of 1,2-benzisoxazole-3-acetamidoxime hydrochloride (PF-257) on the CNS with special reference to monoamine metabolism.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):89P-90P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of 1,2-benzisoxazole-3-acetamidoxime hydrochloride (PF-257) on the brain monoamine metabolism in rats were reported. PF-257, as well as pargyline, antogonized the depletion of brain monoamines, especially that of norepinephrine (NE) which was caused by reserpine, while imipramine enhanced the NE depletion. Doses of PF-257 caused an increase in brain NE, in contrast to the decrease following repeated doses of imipramine. Administration of PF-257 in combination with L-DOPA remarkably and dose relatedly enhanced the increase in brain dopamine (DA) without influencing the level of L-DOPA in the brain. It is concluded that the mechanism underlying the pharmacological effects of PF-257 is the retardation of catecholamine turnover in the central nervous system without inhibiting the enzyme participating in the metabolism of catecholamines, i.e.,monoamine and catechol-O-methyltransferase. (Author abstract modified)

241394 Oka, Tetsuo; Watanabe, Yasuo; Tomizawa, Setsuo. Department of Pharmacology, School of Medicine, Tokai University, Isehara, Kanagawa 259-11, Japan **Effects of environmental temperature on 5-hydroxytryptamine (5-HT) turnover rate in the rat brain (III).** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):90P-91P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effect of high environmental temperature on the turnover of 5-hydroxytryptamine (5-HT) in discrete areas of the rat brain was reported. Concentrations of 5-HT and 5-hydroxyindoleacetic acid (5-HIAA) in brain regions of rats were included. Although 5-HT level of seven discrete areas of the brain of rats exposed to high environmental temperature remained unchanged, 5-HIAA levels of hypothalamus and striatum of rats kept at high environment significantly increased when compared to those of rats placed at room temperature. It is suggested that 5-HT in the hypothalamus and striatum may play an important role in homeostatic responses to heat stress. (Author abstract modified)

241395 Watanabe, Yasuo; Tomizawa, Setsuo; Oka, Tetsuo. Department of Pharmacology, School of Medicine, Tokai University, Isehara, Kanagawa 259-ll, Japan **Drug-induced changes in body temperature and 5-hydroxytryptamine (5-HT) turnover rate in the rat brain.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):91P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of morphine, ketamine, and chlorpromazine, which have been shown to produce hypothermia, on the turnover of 5-hydroxytryptamine (5-HT) in the rat brain were reported. The administration of morphine hydrochloride (HCl), which produced a fall in rectal temperature, significantly increased 5-hydroxyindoleacetic acid (5-HIAA) level in the rat brain. The morphine induced hypothermia was prevented by p-chlorphenylalanine (p-CPA), a specific 5-HT depletor, and restored by the administration of 5-hydroxytryptophan (5-HT) to p-CPA pretreated rats. Thus, the hypothermic response of rats to morphine may depend on the release of 5-HT by morphine. The administration of ketamine-HCl, which caused hypothermia, had essentially no effect on the 5-HIAA level, although the ketamine induced hypothermia was prevented by p-CPA and restored by injection of 5-HTP to p-CPA pretreated rats. The administration of chlorpromazine-HCl produced hypothermia, which was not antagonized by p-CPA, and had essentially no effect on the 5-HIAA level in the rat brain. Thus, drugs, which produce hypothermia in the rat, may be classifed into at least three types in terms of antagonism by p-CPA and 5-HT turnover in the brain. (Author abstract modified)

241396 Sawa, Aiko; Oka, Tetsuo. Department of Pharmacology, School of Medicine, Tokai University, Isehara, Kanagawa 259-11, Japan **Effects of cholinergic drugs on 5-hydroxytryptamine (5-HT) turnover rate in the rat brain.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):91P-92P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of cholinergic drugs on cerebral 5-hydroxytryptamine (5-HT) turnover in the rat brain were reported. The administration of pilocarpine-hydrochloride (HCl) arecoline-HCl or tremorine-2HCl to rats 1 hr before decapitation produced a definite increase in 5-hydroxyindoleacetic acid (5-HIAA) in the brain. In contrast, the 5-HT level was not significantly changed by these cholinergic drugs. The injection of

physostigmine salicylate or nicotine sulfate had essentially no effect on 5-HT and 5-HIAA levels. Atropine sulfate which has essentially no effect on 5-HT and 5-HIAA levels, did not inhibit the increase in 5-HIAA induced by cholinergic drugs. Mecamylamine-HCl which had no significant effects on 5-HT and 5-HIAA levels, did antagonize tremorine induced increase in 5-HIAA levels. Mecamylamine, however, did not inhibit the increase in 5-HIAA levels induced by other cholinergic drugs than tremorine. Thus, although certain muscarinic agonists may activate the serotonergic neuron, a clear relationship between cholinergic and serotonergic neurons could not be demonstrated. (Author abstract modified)

241402 Oka, Tetsuo; Sawa, Aiko. Department of Pharmacology, School of Medicine, Tokai University, Isehara, Kangawa 259-11, Japan **Effects of morphine on 5-hydroxytryptamine (5-HT) turnover in the rat brain (III).** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):97P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effect of morphine on 5-hydroxytryptamine (5-HT) in the rat brain was reported. The concentrations of 5-HT and 5-hydroxyindoleacetic acid (5-HIAA) after administration of morphine hydrochloride (HCl) to p-chlorophenylalanine (p-CPA) pretreated rats were not significantly altered when compared to those after p-CPA alone. Thus, residual 5-HT after the p-CPA injection does not appear to be significantly released by morphine administration. The administration of pargyline, a monoamine oxidase inhibitor, to rats 1 hr before sacrifice, produced definite increases in 5-HT and a significant decrease in 5-HIAA. The magnitude of increase in 5-HT and decrease in 5-HIAA by pargyline was not significantly changed by the morphine administration, although previous results showed that morphine increased 5-HIAA level significantly and a probenecid induced increase in 5-HIAA level was not antagonized by the administration of atropine sulfate, although preliminary experiments showed that cholinergic drugs also increased 5-HIAA level in the rat brain. Thus it appears that morphine does not produce an increase in 5-HIAA through the activation of muscarinic receptor. (Author abstract modified)

241403 Satoh, Hiroko; Kuroiwa, Yukio. Department of Biochemical Toxicology, School of Pharmaceutical Sciences, Showa University, Tokyo 142, Japan **Effect of anti-phenobarbital antibodies on sleeping time induced by cyclobarbital to mice.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):101P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of normal rabbit immunoglobin-G (N-IgG) and phenobarbital specific IgG (Ab-IgG) on cyclobarbital induced sleeping time were reported. Ab-IgG was specifically purified by immunoadsorbent from rabbit antisera obtained by immunization with p-azophenobarbital bovine gamma globulin. N-IgG was purified from normal rabbit sera by DEAE cellulose column chromatography. The aggregates free IgGs were passively immunized to C3H mice at 1 hr before injection with cyclobarbital which has a high binding affinity to the antibodies. Pretreatment with N-IgG significantly prolonged cyclobarbital induced sleeping time as compared with that of the saline treated group, however, in the Ab-IgG treated group, the duration of sleeping time was about the same as that in the saline group. To determine whether or not Ab-IgG has any influence on barbiturate tolerance, the effects of N-IgG and Ab-IgG on the activities of hepatic postmitochondrial enzymes (alkaline RNase and aminopyrine demethylase) of mice were examined 40 hr after cyclobarbital administration. It was found that Ab-IgG has a depressive effect on the induction of the hepatic enzymes compared with N-IgG. (Author abstract modified)

241405 Ito, Nobuyoshi; Akiyama, Ryo; Mori, Masakazu. Department of Pharmacology, Osaka Dental University, Osaka 540, Japan **Effects of barbiturates on blood pressure in lidocaine injected SHR.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):172P-173P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, changes in blood pressure following administration of lidocaine with or without barbiturates in spontaneously hypertensive rats (SHR) and a closely related strain of Kyoto normotensive Wistar rats (NWR) were reported. Systolic blood pressure was indirectly measured with the plethysmographic tail method. This pressure increased after i.p. administration of lidocaine at a dose over 50 mg/kg of body weight. Influence of nine different barbiturates (barbital, phenobarbital, mephobarbital, amobarbital, pentobarbital, secobarbital, hexobarbital, thiopental and thiamylal) orally premedicated was studied for 8 hr after administration of lidocaine. The derivatives dosage was within the nondevelopment of lethargy. Phenobarbital and mephobarbital proved to be most effective. Hexobarbital and thiopental were effective within 3 hr after administration of lidocaine. Amobarbital and secobarbital were slightly effective. Barbital, pentobarbital and thiamylal were not effective in resisting an increase of blood pressure. Phenobarbital and mephobarbital showed a higher median effective dose (ED50) of lethargic action and a more effective anticonvulsant action to lidocaine than did the other seven barbiturates. Primidone used as an anticonvulsant clearly inhibited a systolic pressure increase and convulsion following administration of lidocaine. (Author abstract modified)

241406 Furukawa, Tatsuo; Nakano, Ushio; Ono, Nobufumi. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Fukuoka University, Fukuoka 814, Japan **Modifications of effects of chlorpromazine on adrenergic drugs and barbiturates by repeated administration to rats.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):187P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, modifications of effects of chlorpromazine on adrenergic drugs and barbiturates by repeated administration to rats were reported. The systemic pressure and heartrate responses to i.v. injected adrenergic drugs were measured in male rats. Chlorpromazine (CPZ) or saline as a control was administered daily. The locomotor activities were similarly decreased after the first, fourth, and ninth administration of CPZ. The excitation response in locomotor activities to methamphetamine (MAPT) administered 1 hr after CPZ was markedly reduced, but this antagonistic effect of CPZ was inhibited strongly according to the daily administration of CPZ. Thiopental induced sleeping time was markedly prolonged after CPZ thiopental. This effect tended to be decreased by repeated administration of CPZ. The effects of CPZ on cardiovascular responses to adrenergic drugs, such as adrenaline, noradrenaline, isoprenaline, tyramine and MAPT, were not altered significantly by daily administrations of CPZ. These results suggest that anti-MAPT effects of CPZ are markedly reduced by repeated administration while the potentiative effect on barbiturate hypnosis tends to decrease in rats, and these alterations in the effects of CPZ are weaker in rats than mice. (Author abstract modified)

241414 Alhava, Eeva. Dept. of Pharmacoloy, Univ. of Helsinki, Siltavuornepenger 10, SF-00170 Helsinki 17, Finland **Concentration of amphetamine isomers in brain and heart of adult**

and developing mice. Acta Pharmacologica et Toxicologica (Kobenhavn). 38(4):336n343, 1976.

The levels of d-amphetamine and l-amphetamine in the brain and heart of adult and developing mice aged 3-6 days and 13-16 days were studied. More d-isomer than l-isomer was found in the brain of developing mice, except after a dose of 100mg/kg of the drug, i.e. a dose which produces a higher level of l-amphetamine in the brain of 13-16-day-old mice. Adult brain retained l-amphetamine in a higher concentration than d-amphetamine. In the youngest mice 50mg/kg of the isomers produced equal levels of the drug in the brain and heart, whereas 100mg/kg of the d-form was particularly concentrated in the infant heart. In the older age groups the brain level of either isomer was generally higher than the respective heart level. The importance of peripheral component of amphetamine action in the youngest mice is emphasized, and a low sensitivity of the central nervous system to l-amphetamine in 13-16-day-old as well as in adult mice is revealed. 10 references. (Author abstract)

241416 Hyttel, John. Biochemical Dept., H. Lundbeck & Co. A/S, Ottiliavej 7-9, DK-2500 Valby, Denmark **Effects of a single administration of clozapine on mouse brain catecholamines.** Acta Pharmacologica et Toxicologica (Kobenhavn). 38(4):358-365, 1976.

The effects of clozapine on the accumulation and disappearance of 14C-labelled catecholamines formed from 14C-tyrosine, and on the endogenous levels of catecholamines were studied in mouse brain. Rather low doses of clozapine increased noradrenaline accumulation and disappearance (from 2.5and 0.16mg/kg, respectively), whereas dopamine accumulation was only increased from 10mg/kg and disappearance after 80mg/kg. However, in the dosage interval of 1.25 to 5mg/kg dopamine disappearance was decreased. Endogenous noradrenaline levels were decreased from 10mg/kg in contrast to the dopamine levels which remained unchanged, except in the dosage interval 2.5to 10mg/kg, where they were elevated, at the same time at which dopamine disappearance was decreased. It is concluded that clozapine differs biochemically from the typical neuroleptics by changing the metabolism of noradrenaline in doses much lower than those influencing dopamine metabolism. It is suggested that this property, together with the ability of clozapine to decrease dopamine disappearance in a certain dose range, could contribute to the unique psychopharmacological action of clozapine. 16 references. (Author abstract)

241573 Browne, Ronald Gregory. University of Texas Health Science Center, Houston Graduate School of Biochemical Sciences **The role of serotonin in the discriminative stimulus properties of mescaline. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-4548 HC$18.00 MF$7.50 89 p.

In order to elucidate the role of serotonin in the mechanism of action of mescaline, male Sprague-Dawley rats were trained to discriminate intraperitoneally administered mescaline hydrochloride from saline in a two lever operant chamber for food reinforcement. Reward was contingent upon responses made greater than 15 sec apart on the appropriate lever paired with either drug or saline administration. The generalization gradient produced by mescaline was dose dependent and the time course generalization correlated with peak brain levels of 14C-mescaline. Stimulus generalization produced by mescaline was analyzed in rats treated with blockers of both peripheral and central serotonin (5-HT) receptors (cinanserin, methysergide, or cyproheptadine) and results suggest that mescaline produces its discriminative effects by stimulating central serotonergic receptors. Further tests indicate that discriminative cue produced by mescaline is a concomitant of direct central nervous system serotonergic receptor stimulation and suggest that supersensitivity may develop to the effects of mescaline after a reduction in brain 5-HT levels. The specificity of the behavioral paradigm was tested with another group of rats trained to discriminate pentobarbital from saline. Pretreatment with the 5-HT receptor blockers and parachlorophenylalanine did not alter the discriminability of pentobarbital. These results demonstrate that the use of drug discrimination paradigms provides a highly specific and quantitative behavioral method for elucidating the mechanism of action of drugs. (Journal abstract modified)

241574 Hruska, Robert Edward. University of Arizona **The behavioral and neuropharmacological effects of taurine. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-2545 HC$18.00 MF$7.50 141 p.

The behavioral and neuropharmacological effects of taurine were investigated in the mouse following an intraperitoneal injection. The injection produces a dose related decrease in temperature, conditioned drinking and conditioned eating. The extent of hypothermia after injection was the same at a room temperature of 5 degrees C or 23 degrees C. Even a small decrease in body temperature occurred at a room temperature of 36 degrees C. Taurine also produced a hypothermia in 6-hydroxydopamine pretreated mice or in adrenalectomized mice. It is concluded that taurine, after intraperitoneal injection, only decreases behaviors mediated by the hypothalamus. The actual mechanism by which taurine produces such effects is not known. However, the hypothalamic effects of taurine do not involve peripheral adrenergic or cholinergic systems, central cholinergic systems, any system affected by amphetamine, or biogenic amines in the hypothalamus. (Journal abstract modified)

241575 Milloy, Svetlana. City University of New York **Tolerance to the activity-enhancing effect of d-amphetamine. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-3824 HC$18.00 MF$7.50 149 p.

The problem of tolerance development to the activity enhancing effect of d-amphetamine in the mouse and rat was examined. The criterion employed to ascertain the existence of tolerance was the shifting of the dose/response curve to the right. It was demonstrated that tolerance occurred when mice were tested with d-amphetamine in activity boxes following 7 days of drug injections. The number of drug injections and the interval between drug injections were shown to be important factors. Tolerance to d-amphetamine also occurred in mice following 7 days of testing with the drug, however, it failed to develop when mice were tested with d-amphetamine daily for 3 days, and when mice were tested twice daily with the drug for 3.5days. Behavioral and environmental variables were also shown to affect tolerance development in the mouse. In contast to the results obtained with mice, rats receiving seven daily injections of d-amphetamine, either with or without concurrent activity testing, were found to be more sensitive rather than tolerant to d-amphetamine. This heightened sensitivity was related to a persistent metabolite of d-amphetamine. Rats which were tested without drug for 7 days were less sensitive when tested with d-amphetamine than were rats which had received chronic drug injections. Implications of the results are discussed in terms of the catecholamine hypothesis of affective disorders and amphetamine induced psychosis in man. (Journal abstract modified)

241576 Riffee, William Harvey. Ohio State University **The effect of acute and chronic amphetamine administration on seizure susceptibility and brain catecholamines in mice. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-3533 HC$18.00 MF$7.50 255 p.

The effects of acute and chronic amphetamine administration on seizure susceptibility and brain catecholamines in mice were investigated. Acute administration of (+)-amphetamine and (-)-amphetamine increased susceptibility to low frequency electroshock and pentylenetetrazol (PTZ) induced clonic seizures in ICR mice. The (+)- isomer decreased and the (-)-isomer increased susceptibility of ICR mice to PTZ induced tonic seizures. After chronic administration of these isomers of amphetamine, tolerance developed to all the effects observed upon acute administration in this strain. The acute administration of (-)-amphetamine resulted in a decrease in PTZ induced clonic seizure susceptibility in CD-1 and CF-1 mice. Neurochemical studies and investigations utilizing noradrenergic and dopaminergic blocking agents in CD-1 mice suggested the interactions of the (-)-isomer with norepinephrine (NE) and dopamine (DA) were very complex. These interactions may have involved increased alpha-adrenergic and beta-adrenergic receptor NE as well as dopaminergic receptor DA interactions. A decrease in dopaminergic neuronal activity may also have been involved. Chronic administration of (+)-amphetamine in CD-1 mice produced no tolerance to the observed decrease in PTZ seizure susceptibility. There was, however, an indication of increased noradrenergic activity as well as noradrenergic receptor subsensitivity after chronic administration of this dose. A withdrawal syndrome, characterized by an increase in PTZ induced clonic seizure susceptibility, was observed at 12 hour intervals up to 48 hours after cessation of chronic (+)-amphetamine administration. Tolerance did develop to the effect of (+)-amphetamine to increase seizure susceptibility after chronic administration of this dose to CD-1 mice. There were also indications of a decrease in the magnitude of noradrenergic activity and the development of noradrenergic and dopaminergic receptor subsensitivty. A withdrawal syndrome, characterized by a decrease in seizure susceptibility, was observed at 12 hour intervals up to 48 hours after cessation of chronic administration of the higher dose of the (+)-isomer. (Journal abstract modified)

241678 Farber, Jorgel. City University of New York **The effects of unilateral locus coeruleus lesions on hypothalamic intracranial self-stimulation and sleep in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-3816 HC$18.00 MF$7.50 240 p.

The role of the nucleus locus coeruleus (LC) of the pons in intracranial self-stimulation (ICSS) and sleep was investigated in rats implanted with ICSS electrodes aimed at the LC, hypothalamus, and substantia nigra. One group of subjects was also implanted with electroencephalogram (EEG) and electromyogram (EMG) electrodes. This group underwent a sleep drug paradigm which tested the effects of d-amphetamine and l-amphetamine on hypothalamic ICSS before and after the LC lesion, and the effects of this lesion on the sleep cycle. Results show that distant and discrete unilateral lesions can reduce and abolish ICSS behavior. Thus, the central reward system is not redundant and capable of recovery. Furthermore, the differential LC lesion effects on hypothalamic ICSS demonstrate that the hypothalamus is not a unitary ICSS center, but rather a site that receives inputs from different ICSS systems. Prelesion d-amphetamine was more effective in enhancing ICSS from sites that were detrimentally affected by the LC lesion than those that were not; prelesion l-amphetamine had no differential effects. Postlesion d-amphetamine, but not l-amphetamine, returned reduced ICSS rates and decreased ICSS threshold to prelesion levels. Given that unilateral lesions of the noradrenergic LC either abolish or drastically reduce ICSS from sites rich in dopamine, it is postulated that ICSS from the noradrenergic dorsal bundle and the dopaminergic nigrostriatal system depend on the integrity of the LC. (Journal abstract modified)

241798 Fock, Sibylle; Mense, Siegfried. Physiologisches Institut der Universitat, Lehrstuhl I, D-2300 Kiel, Germany **Excitatory effects of 5-hydroxytryptamine, histamine and potassium ions on muscular group IV afferent units: a comparison with bradykinin.** Brain Research (Amsterdam). 105(3):459-469, 1976.

The excitation of muscular group IV afferent units by the pain producing substances 5-hydroxytryptamine (5-HT), histamine, and potassium ions was studied in cats and compared with the bradykinin effects of an earlier investigation. The substances were injected into the sural artery, and the action potentials of single group IV afferent fibers from the gastrocnemius soleus muscle were recorded extracellularly. About half of the 180 units tested with chemical stimulation could be excited by amounts of the above agents which are likely to be present in pathologically altered tissues. Of the tested substances, 5-HT was the most and potassium the least effective stimulant; in comparison with bradykinin, 5-HT was by far less potent. The threshold injection doses of potassium chloride (KCl) for activation of muscular group IV units were such that an unspecific depolarizing mode of action seems probable. 22 references. (Author abstract modified)

241805 Raabe, W.; Ayala, G. F. Dept. of Neurology, St. Paul-Ramsey Hospital, St. Paul, MN 55101 **Diphenylhydantoin increases cortical postsynaptic inhibition.** Brain Research (Amsterdam). 105(3):597-601-1976.

The effect of diphenylhydantoin (DPH), administered intravenously with an infusion pump, on the electrophysiological activity of the motor cortex was investigated in the cat. Extracellular recordings were obtained from pyramidal tract cells; an electrocorticogram was monitored by means of a silver ball electrode on the anterolateral sigmoid gyrus. The experiments demonstrate an increase of cortical inhibition, as measured by the suppression of antidromic action potentials. Because DPH prolongs the hyperpolarization produced by inhibitory postsynpatic potentials (IPSPs), it is proposed that it also inhibits orthodromic action protentials and excitatory postsynaptic potentials (EPSPs). It is concluded that the ability of DPH to prolong the inhibition of action potentials and EPSPs by increasing the duration of the hyperpolarization of the IPSP may explain some aspects of its action as an anticonvulsant. It is noted that interactive effects of DPH with Nembutal (pentobarbital sodium) cannot be ruled out. 26 references.

241919 Dorris, R. L.; Shore, P. A. Department of Pharmacology, University of Texas Health Science Center, Dallas, TX 75235 **On the mechanism of action of clozapine on the adrenergic neurone.** British Journal of Pharmacology (London). 56(3):279-283, 1976.

The effect of clozapine on peripheral adrenergic neurons of the rat heart is examined. It is shown that the drug lowers the concentration of heart noradrenaline and also releases the non-metabolizable false adrenergic transmitter, metaraminol, by a nerve impulse dependent mechanism. It is also shown that, unlike other alpha-adrenoceptor blocking drugs or antipsychotic drugs tested, clozapine appears to exert a further action directly on the adrenergic neuron so as to facilitate impulse

dependent amine release. 16 references. (Author abstract modified)

241920 Rivera-Calimlim, Leonor. Department of Pharmacology and Toxicology, University of Rochester, School of Medicine and Dentistry, Rochester, NY 14642 **Impaired absorption of chlorpromazine in rats given trihexyphenidyl.** British Journal of Pharmacology (London). 56(3):301-305, 1976.

The absorption and tissue distribution of orally administered (14C)-chlorpromazine (CPZ) were compared in trihexyphenidyl (THP; Artane) treated and control rats. Total radioactivity (CPZ) in the plasma and brain of rats treated with THP was significantly lower and total radioactivity in the stomach significantly higher than in rats not previously treated with THP. Gastric emptying in rats treated with THP was significantly delayed as measured by gastric clearance of a marker, (14C)-polyethylene glycol. Transport of (14C)-CPZ in everted sacs was not affected by treatment with THP. Metabolism of (14C)-CPZ by liver homogenates was not affected by treatment with THP. The relationship of delayed gastric emptying in THP treated rats and their lower plasma and brain levels of (14C)-CPZ after oral administration is discussed. 14 references. (Author abstract)

241921 Curtis, D. R.; Game, C. J. A.; Lodge, D. Department of Pharmacology, Australian National University, Canberra, Australia **Benzodiazepines and central glycine receptors.** British Journal of Pharmacology (London). 56(3):307-311, 1976.

The possible interaction between diazepam, strychnine and glycine in vivo was examined. In cats, intravenous diazepam enhanced dorsal root potentials but did not significantly diminish the reduction by electrophoretic strychnine of the inhibitory action of electrophoretic glycine on dorsal horn interneurons. In mice, intraperitoneal diazepam had no appreciable effect on the potency of strychnine as a convulsant, although some protection against bicuculline was provided. These observations, together with the failure of chlordiazepoxide to either inhibit the firing of spinal interneurons or reduce antagonism between strychnine and glycine when administered locally, provide no support for the interaction between benzodiazepines and mammalian central glycine receptors which has been proposed on the basis of in vitro studies of strychnine binding. 11 references. (Author abstract modified)

241922 Nistri, A. Institute of Pharmacology, University of Florence, Italy **Effects of morphine on acetylcholine release from the frog spinal cord.** British Journal of Pharmacology (London). 56(3):352P, 1976.

The frog spinal cord was chosen as an in vitro central nervous system preparation to study the effects of bath applied morphine on spinal root potentials and endogenous acetylcholine (ACh) release. Since small concentrations of morphine depressed spontaneous ACh output but failed to reduce the electrically evoked ACh output, it is suggested that morphine reduced ACh release through an indirect mechanism probably mediated by interneurons. It is proposed that the stimulant action of high concentrations of morphine on spinal ACh release and root potentials is one of the factors involved in the behavioral excitation seen in frogs after large doses of this opiate. 5 references.

241923 Barasi, S.; Parry, O.; Roberts, M. H. T. Department of Physiology, University College, Cardiff, Wales **The interpretation of responses of motoneurone field potentials to 5-hydroxytryptamine.** British Journal of Pharmacology (London). 56(3):366P-367P, 1976.

Various responses of motoneuron field potentials to 5-hydroxytryptamine in rats are evaluated. To assist with the interpretation of changes in the field potential amplitude, glycine, glutamate and potassium were applied by iontophoresis into the ventral horn. The results are compatible with the suggestion that an increased field potential amplitude may be an index of increased motoneuron excitability. A further test of this postulate involved stimulating the ventral root or muscle nerve with three to six stimuli at 80 to 200 Hz. The field potential progressively declined in amplitude during the train. These results offer additional support for the postulate that motoneuron excitability is increased by these drugs. 8 references.

241924 Goodlet, I.; Mireylees, S. E.; Sugrue, M. F. Department of Pharmacology, Organon Scientific Development Group, Newhouse, Lanarkshire ML1 5SH, England **The selective inhibition of 5-hydroxytryptamine re-uptake by Org 6582.** British Journal of Pharmacology (London). 56(3):367P-368P, 1976.

In vivo blockade of 5-hydroxytryptamine (5-HT) was studied by investigating the effect of drug pretreatment on the ability of p-chloroamphetamine to lower rat brain 5-HT. Intraperitoneally administered Org-6582 (dl-8-chloro-11-anti-amino-benzo-(b)-bicyclo (3.3.1) nona-3,6a (10a) diene hydrochloride) was approximately twice as potent as fluoxetine, five times more potent than chlorimipramine and 14 times more potent than desipramine in blocking the ability of p-chloroamphetamine to lower brain 5-HT content. Peripheral in vivo blockade of noradrenergic reuptake was also determined. The results indicate that Org-6582 is a potent selective inhibitor of 5-HT reuptake. 3 references.

241925 Curzon, G.; Marsden, C. A. Department of Neurochemistry, Institute of Neurology, Queen Square, London WC1N 3BG, England **Effect of LSD on rat brain 5-hydroxytryptamine metabolism at elevated environmental temperature.** British Journal of Pharmacology (London). 56(3):368P-369P, 1976.

The effects of a 40 degrees C environment on tryptophan disposition and on brain 5-hydroxytryptamine (5-HT) metabolism and their modification by lysergic acid diethylamide (LSD) are reported. The results of experiments indicate that the increase in 5-hydroxyindoleacetic acid in rats exposed to 40 degrees C is not obviously related to increased plasma and brain tryptophan. LSD appeared to decrease catabolism of 5-HT formed from exogenous tryptophan at 40 degrees C. If this, like the decreased catabolism of endogenous 5-HT after LSD, is caused by decreased release of 5-HT at the synapse, then it implies that exogenous tryptophan can cause increased 5-HT release. Other findings are in agreement. 6 references.

241926 Littleton, J. M.; Maclean, K. I. Department of Pharmacology, King's College, London WC2, England **Alterations in dopamine uptake in rat corpus striatum induced by combinations of stress and delta8-tetrahydrocannabinol (delta8-THC).** British Journal of Pharmacology (London). 56(3):370P, 1976.

Environmental alteration of the effect of delta8-tetrahydrocannabinol (THC) on rat striatal dopamine uptake was examined. Male Wistar rats were kept under normal conditions for 14 days before every experiment. Rats under stressful conditions were isolated with access to water but not food for 24 hours before being killed. Environmental temperature was 21 degrees C; the lighting cycle was 12 hours light and 12 hours dark. The results explain previous findings that striatal dopamine depletion after inhibition of dopamine synthesis was

reduced by delta8-THC only in stressed animals. The experiments also provide important evidence for the alteration by stress of the biochemical effects of delta8-THC. When delta8-THC was administered in a stressful environment it caused an apparent increase in striatal dopamine uptake. This change implicates central dopaminergic function in the abnormal behavior patterns induced by delta8-THC when administered to stressed animals. 5 references.

241929 Donaldson, I. M.; Jenner, P.; Marsden, C. D.; Miller, R.; Peringer, E. University Department of Neurology, Institute of Psychiatry, London SE5 8AF, England **Is metoclopramide a directly acting dopamine receptor antagonist?** British Journal of Pharmacology (London). 56(3):373P, 1976.

The action of metoclopramide on cerebral dopamine (DA) receptors was examined in experiments with mice. The data suggest that the blockade of DA receptors observed following administration of metaclopramide is due to a specific central action of the drug itself, rather than to a peripheral metabolite. The failure of metoclopramide to inhibit the DA sensitive adenylate cyclase system in vitro suggests a mode of action differing from that of antipsychotic drugs. Whether this represents an action on other DA receptors not tested by the in vitro system or an effect on another neuronal system remains to be determined. 4 references.

241930 Candy, J. M.; Key, B. J. M.R.C. Neuropharmacology Unit, Medical School, Birmingham B15 2TJ, England **Blockade of the electrocortical changes induced by perfusion of amphetamine in the brain stem reticular formation.** British Journal of Pharmacology (London). 56(3):374P, 1976.

The effect of bilateral perfusion for 5 min of (+)-amphetamine into the mesencephalic reticular formation (MRF) of 30 cat encephale isole preparations was investigated. The results suggest that amphetamine has a presynaptic action on noradrenaline (NA) terminals within the MRF and that the NA terminals, although depleted, are still capable of taking up exogenously applied NA or alpha-methyl-noradrenaline after a 1 hour perfusion of 6-hydroxydopamine. Histochemical data support the pharmacological results. 2 references.

241931 Youdim, M. B. H. M.R.C. Clinical Pharmacology Unit, Radcliffe Infirmary, Oxford OX2 6HE, England **Monoamine oxidase active site; the binding to and titration of monoamine oxidase with (14C)-selective inhibitors.** British Journal of Pharmacology (London). 56(3):375P, 1976.

The action of monoamine oxidase (MAO) is examined with regard to 14C selective inhibitors. It is suggested that certain physiological factors influence the activity of MAO, which in turn may affect monoamine metabolism. It is proposed that the changes in enzyme activity are due to a change in MAO protein synthesis or degradation. In experimental studies and disease states in the human where MAO activity fluctuates it is desirable to know the exact amount of enzyme present. The results indicate the use of labeled selective inhibitors as agents for titration of MAO and its multiple forms because the inhibition is stoichiometric and the titration endpoint can be used to estimate the enzyme concentration. 5 references.

241978 Marley, E.; Whelan, Jennifer E. Department of Pharmacology, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, England **Some pharmacological effects of p-chlorophenylalanine unrelated to tryptophan hydroxylase inhibition.** British Journal of Pharmacology (London). 56(2):133-144, 1976.

The properties of p-chlorophenylalanine methyl ester (PCPA) are compared with those of 5-hydroxytryptamine (5-HT) on a variety of different species such as the rat, guinea-pig, and cat. PCPA, like 5-HT, contracted the rat fundal preparation; in cats, enhanced twitch tension of a lower limb flexor reflex, evoked adrenal medullary secretion, and attenuated histamine induced gastic secretion. The effects on the rat fundal strip and the adrenal medulla were prevented by methysergide. Like 5-HT, PCPA elicited bronchoconstriction of guinea-pig lungs, isolated or in vivo. This was not prevented by methysergide but reduced by polyphloretin and by indomethacin. Perfusate collected from the lungs during PCPA induced bronchonconstriction and applied to superfused isolated tissues contained a substance with prostaglandin like activity. In contrast, the effect of PCPA on the guinea-pig isolated ileum differed from that of 5-HT, since it relaxed the ileum when contracted by transmural excitation, by acetylcholine, histamine or 5-HT and contracted the ileum on washout. 34 references. (Author abstract modified)

241980 Komissarov, I. V.; Talalayenko, A. N. Kafedera farmkologii Donetskogo meditsinksogo instituta, Donetsk, U.S.S.R. **/On monoaminergic mechanisms of the amygdala complex implementing conditioned reflexes of various biological modalities./** O monoaminergicheskikh mekhanizmakh mindalevidnogo kompleksa, realizuyushchikh uslovnyye refleksy razlichnoy biologicheskoy modal'nosti. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 80(11):3-5, 1975.

The functional significance of norepinephrine, dopamine, and serotonin introduced into the dorsomedial regions of the rat amygdala complex was investigated. Microinjection of dopamine and serotonin increased the latent period of conditioned defense and motor food reactions, spontaneous motor activity, the number of jerks, and the value of the conditioned food reflex. Norepinephrine failed to influence the recorded indices of the conditioned food procuring reflex, but it facilitated the conditioned reaction of avoidance, significantly shortening its latency. Results indicate the specificity of the neurochemical mechanisms in the rat at this level. 13 references. (Journal abstract modified)

241986 Lyubimov, B. I.; Pentyuk, A. A.; Rybak, P. G.; Samoylov, N. N. Institut farmakologii AMN SSSR, Moscow, U.S.S.R. **/Effect of lithium chloride on lipid metabolism./** Vliyaniye khlorida litiya na lipidnyy obmen. Farmakologiya i Toksikologiya (Moskva). 29(1):53-56, 1976.

Lithium chloride was injected subcutaneously in mice (500 or 300mg/kg) once a day for 10 and 15 days, and to rabbits in single doses via a tube into the stomach (400 or 850mg/kg). After different time intervals following single dose or series administration of the compound, the level of total lipids was determined in the muscles and liver of the mice; the level of total lipids, beta-lipoproteins, phospholipids, cholesterol, fatty acids, and 11-oxycorticosteroids was determined in the blood serum of the rabbits; and the bile acid content in the vesical bile of these animals was assessed. It is suggested that the hyperlipemia observed after lithium is caused by mobilization of fat from fat deposits and by disturbed interstitial lipid metabolism. 10 references. (Journal abstract modified)

241987 Barkov, N. K.; Nesmelov, N. B. Laboratoriya farmakologii nervnoy sistemy Instituta farmakologii AMN SSSR, Moscow, U.S.S.R. **/Change in ethanol consumption by albino rats under the effect of neuroleptics and tranquilizers./** Izmeneniye potrebleniya etanola belymi krysami pri deystvii neyroleptikov i trankvilizatorov. Farmakologiya i Toksikologiya (Moskva). 39(1):5-9, 1976.

The possibility of changing ethanol consumption in albino rats by using preparations having a primarily tranquilizing and antipsychotic action was studied. Selective consumption of ethanol solutions by means of multiple parenteral introduction of the compound was developed. Both diazepam and neuroleptic agents depressed selective consumption of ethanol. Differences in the action of the preparations and their possible use in the treatment of alcoholism are discussed. 9 references. (Journal abstract modified)

241988 Medvedev, O. S.; Stepochkina, N. A. Kafedra farmakologii, I Leningradskogo meditsinskogo instituta imeni I. P. Pavlova, Leningrad, U.S.S.R. **/Effect of amphetamine and gutimin on adaptive changes in arterial pressure arising in response to contraction of the skeletal muscles./** Vliyaniye fenamina i gutimina na adaptatsionnyye izmeneniya arterial'nogo davleniya, voznikayushchiye pri sokrashchenii skeletnykh myshts. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 80(12):41-44, 1975.

The influence of amphetamine (0.1-11mg/kg) and gutimin (5-50mg/kg) on the pressor reflex originating in the muscle during exercise was investigated in nonanesthetized decerebrate cats. Isometric exercise of the hind limb muscles was elicited by stimulating spinal ventral roots L6-A1. Amphetamine in a dose of 0.1mg/kg increased the level of arterial pressure and the amplitude of the pressor reflex. Higher doses decreased the pressor reflex to exercises, and a fall in arterial pressure was observed. Gutimin elevated the arterial pressure and failed to alter the pressor reflex to exercises. 12 references. (Journal abstract modified)

241989 Lyubimov, B. I.; Markin, V. A.; Mitrofanov, V. S. Laboratoriya obshchey farmakologii Instituta farmakologii AMN SSSR, Moscow, U.S.S.R. **/Histotopography of the changes in enzyme activity in the rat brain under the effect of fluorophenazine./** Gistotopografiya izmeneniy fermentativnoy aktivnosti v golovnom mozge krys pod vliyaniyem ftorfenazina. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 80(12):38-41, 1975.

The effect of fluorophenazine on succinic acid and citric acid reduced nicotinamide adenine dinucleotide and reduced nicotinamide adenine dinucleotide phosphate dehydrogenases in different brain structures was investigated using histochemical methods in 30 white rats. Enzymatic activity was the greatest in the limbic and frontal regions of the cortex 3 hours after administration of a single, subcutaneous injection of fluorophenazine (1 and 5mg/kg). In these structures the inhibitory effects of fluorophenazine were greater than those of the neuroleptics trifluoroperazine and chlorpromazine. The interest of the histotopographical peculiarities of the inhibitory influence of fluorophenazine on enzyme activity is emphasized from the standpoint of the selective activity of the preparation. 7 references. (Journal abstract modified)

242200 Shudo, Isami; Saito, Hideya; Tanabe, Tsuneyoshi. Dept. of Pharmacology, Hokkaido University School of Medicine, Sapporo 060, Japan **The modification of inotropic action of ouabain by 6-hydroxydopamine and alpha-methyl-p-tyrosine in dogs.** Japanese Journal of Pharmacology (Kyoto). 25(6):639-643, 1975.

The action of ouabain on myocardial inotropism pretreated with 6-hydroxydopamine and alpha-methyl-p-tyrosine was studied in dogs. Inotropic action of ouabain was not changed by depletion of catecholamines in the brain, in which the central sympathetic neurons were destroyed by an intraventricular administration of 6-hydroxydopamine. Systemic administration of 6-hydroxydopamine and alpha-methyl-p-tyrosine reduced ventricular catecholamines to 5.3% and 20.8% of the control, respectively. Percent increase of contractility by ouabain after the pretreatment of 6-hydroxydopamine and alpha-methyl-p-tyrosine was reduced to 16.7% and 50.2% of the control, respectively. The results obtained suggest that catecholamines in the myocardium play some important role in producing cardiotonic action of cardiac glycosides. Brain catecholamines or the central sympathetic nervous system do not appear to participate in the exertion of the positive inotropic action of cardiac glycosides. 18 references. (Author abstract)

242201 Satoh, Hiroko; Kuroiwa, Yukio. Dept. of Biochemical Toxicology, School of Pharmaceutical Sciences, Showa Univ., Shinagawa-ku, Tokyo 142, Japan **Effects of passive immunization with rabbit anti-phenobarbital IgG on cyclobarbital-induced sleeping time and hepatic enzyme activities of C3H mice.** Japanese Journal of Pharmacology (Kyoto). 25(6):645-652, 1975.

The effects of normal rabbit IgG (N-IgG) and phenobarbital specific IgG (Ab-IgG) on cyclobarbital induced sleeping time were studied. Ab-IgG was specifically purified from rabbit antisera obtained by immunization with p-azophenobarbital bovine gamma-globulin. N-IgG was purifed from normal rabbit sera by diethylaminoethanol cellulose chromatography. The aggregate free IgG was passively immunized to C3H mice an hour before intraperitoneal injection of cyclobarbital which has a high binding affinity to the antibodies. The pretreatment with N-IgG prolonged significantly cyclobarbital induced sleeping time as compared with that of saline treated group; however, in the Ab-IgG treated group the duration of the sleeping was much the same as that seen in the saline group. To determine whether Ab-IgG has any influence on barbiturate tolerance, effects of N-IgG and Ab-IgG on the activities of hepatic enzymes were examined at 40 hours after cyclobarbital administration. The activities of both enzymes which could be induced by cyclobarbital were decreased significantly in the Ab-IgG treated group as compared with those of the N-IgG group. These results are discussed in relation to barbiturate tolerance. 19 references. (Author abstract)

242202 Sakurada, Tsukasa; Onodera, Kenji; Tadano, Takeshi; Kisara, Kensuke. Dept. of Clinical Pharmacology, Tohoku College of Pharmacy, Komatsushima, Sendai 983, Japan **Effects of polyamines on the central nervous system.** Japanese Journal of Pharmacology (Kyoto). 25(6):653-661, 1975.

The effects of polyamines on the central nervous system were studied in mice. Intraperitoneal administration of spermidine (SPD) and spermine (SPM) decreased spontaneous motor activity as measured by either the photocell counters method or the open-field test and lowered rectal temperature. A significant prolongation of sleeping time after pentobarbital was confirmed in small doses of SPD and SPM which had slight influence on spontaneous motor activity. The time to convulsion and death induced by strychnine was elongated by SPD and SPM. SPM in small doses inhibited writhing responses induced by 0.7% acetic acid. In addition, methampetamine induced hyperactivity and conditioned avoidance responses were blocked by SPM in doses which decreased spontaneous motor activity. In all experiments, SPM appeared to have a powerful pharmacological activity compared with SPD. The LD50s for SPD and SPM were 620 (500-769) mg/kg i.p. and 310 (200-480) mg/kg i.p.,respectively. 22 references. (Author abstract)

242204 Misu, Yoshimi; Kuraishi, Yasushi; Takagi, Hiroshi. Dept. of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto Univ., Sakyo-Ku, Kyoto 606, Japan **Pre- and post-synaptic origin of lithium-induced acute blockade on adrenergic transmission in rabbit heart.** Japanese Journal of Pharmacology (Kyoto). 25(6):787-790, 1975.

The action of lithium on adrenergic transmission in perfused rat hearts was investigated with sympathetic trunks as a model. Results suggest that the major mechanism of transmission blockade induced by lithium is of postsynaptic origin and that lithium increases noradrenaline uptake by adrenergic endings in the heart, which results in a decrease in the transmitter available for interaction with receptors. It is concluded that the primary blocking action of lithium on the adrenergic transmission is not due to a decrease in noradrenaline which interacts with receptors, but rather to an inhibition of postsynaptic responses of rabbit heart to the transmitter. 12 references.

242544 Allikmets, L. Kh.; Zharkovskiy, A. M. Kafedra farmakologii, Tartuskogo universiteta, Tartu, U.S.S.R. **/Participation of the serotonergic system of the brain in the regulation of emotional reactivity./** Uchastiye serotoninergicheskoy sistemy mozga v regulyatsii emotsional'noy reaktivnosti. Zhurnal Vysshey Nervnoy Deyatel'nosti imeni. I. P. Pavlova (Moskva). 25(6):1284-1291, 1975.

Vocalization and aggression reactions produced by electric shock stimulation were investigated in experiments on male Wistar rats. The effect of serotonergic and dopaminergic drugs on emotional reactivity and serotonin metabolism was studied in parallel experiments. The results indicate that l-tryptophan depresses while L-dopa intensifies emotional reactivity and aggressiveness, with L-dopa lowering the level of endogenous serotonin and enhancing its catabolism. L-dopa, d,l-amphetamine, alpha-methyl-Dopa, parachlorophenylalanine, and the serotonin blocking agents deseryl and lysergide eliminated the tranquilizing action of tryptophan on emotional reactivity, decreasing serotonin accumulation and intensifying the formation of 5-hydroxyindoleacetic acid. 30 references. (Journal abstract)

242736 Veale, W. L.; Whishaw, I. Q. Div. of Medical Physiology, Univ. of Calgary, 2920 24th Avenue, NW, Calgary, Alberta, T2N 1N4, Canada **Body temperature responses at different ambient temperatures following injections of prostaglandin E1 and noradrenaline into the brain.** Pharmacology, Biochemistry and Behavior. 4(2):143-150, 1976.

Since prostaglandins of the E series (PGE-1) have been implicated in the production of fever by pyrogens, they were applied directly to the anterior hypothalamic preoptic area of unanesthetized rats at various temperatures. The region of the brain of the rat from which temperature responses can be produced by local injection was determined. Evidence is also presented to suggest that the responses to local injections of PGE-1 are relatively unaffected by environmental temperatures, whereas those in response to injections of noradrenaline are influenced by ambient temperature. These results are discussed in light of similar findings with respect to the response to pyrogens in that it is relatively unaltered by ambient temperature. This work lends further support to the hypothesis that pyrogens act in the hypothalamus by releasing prostaglandins. 25 references. (Author abstract)

242741 LeBlanc, A. E.; Matsunaga, M.; Kalant, H. Addiction Research Foundation, 33 Russell Street, Toronto, Ontario, Canada M5S 2S1 **Effects of frontal polar cortical ablation and cycloheximide on ethanol tolerance in rats.** Pharmacology, Biochemistry and Behavior. 4(2):175-179, 1976.

The effect of bilateral frontal polar cortical ablations and of cycloheximide, an inhibitor of protein synthesis, on the ability of rats to become tolerant to ethanol is reported. Of a group of 30 adult male Wistar rats, only the lesioned group failed to reacquire tolerance. A pilot experiment showed that occipital cortical ablations also prevented tolerance. In a second experiment, 32 rats, which had similarly undergone and then recovered from an initial period of ethanol tolerance, were divided into four groups which received daily treatment with sucrose plus cycloheximide, sucrose plus saline, ethanol plus cycloheximide, and ethanol plus saline, respectively. Only the ethanol plus saline group reacquired tolerance. It is concluded that frontal polar cortical lesions and cycloheximide can both block the development of tolerance to ethanol in animals previously shown to be capable of developing such tolerance. 19 references. (Author abstract modified)

04 MECHANISM OF ACTION: BEHAVIORAL

238687 Chapman, Carol R.; Sparber, S. B. Department of Pharmacology, University of Minnesota, Minneapolis, MN 55455 **Prevention of reversal of operant behavioral disruption during precipitated withdrawal by treatment with morphine before or after naloxone.** Federation Proceedings. 35(3):265, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, prevention or reversal of operant behavioral disruption during precipitated withdrawal by treatment with morphine (M) before or after naloxone (Nx) was reported in rats. Rats, stabilized on a fixed-ratio-20 schedule of reinforcement (food), had their behavior sampled duing 5 min periods once per hr for 5 hr. After M or placebo pellet implantation they were given M sulfate, saline (S) or handled, but non injected (X), 30 min before the 2nd period. NxHCl or S was also administered 5 min prior to the same period. Following condition X, rats were always given Nx 5 min prior to period 2 and M 30 min before period 3. The N-Nx-M treatment showed behavioral disruption after Nx and abrupt reversal after M in the dependent rats while the placebo group exhibited no change in the operant following Nx but a slight suppression after M. Changes in body weight were recorded and reflect the same trends. (Journal abstract modified)

238694 Brocco, M. J.; Slikker W., Jr. Department of Pharmacology, School of Medicine, University of California, Davis, CA 95616 **Responses of normal and isolate monkeys to d-amphetamine, cocaine, chlorpromazine and diazepam.** Federation Proceedings. 35(3):268, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the responses of normal and isolate monkeys to d-amphetamine, cocaine, chlorpromazine and diazepam were reported. Behavioral repertoires of four adult female rhesus monkeys raised in isolation (Group I) were compared to those of four adult females normally raised (Group II). Following the establishment of baselines the animals were administered drugs: d-amphetamine, cocaine, chlorpromazine and diazepam. With both stimulants, more clearly with amphetamine, Group I exhibited predominantly changes in the psychological repertoires whereas Group II exhibited changes confined to neurologic signs. Under chlorpromazine indifference to the environment, reduction of apprehension or of aggressiveness and sedation were observed in all animals of Group I. Group II did not present the same homogeneity of response. Diazepam produced its well-known

"taming effect" with sedation and some ataxia in all animals. Group I exhibited a selective increase in hyperreactivity induced by environmental changes of monkey origin. (Journal abstract modified)

238696 Schlemmer, R. F., Jr.; Jackson, J. A.; Preston, K. L.; Bederka, J. P., Jr.; Garver, D. L.; Davis, J. M. University of Illinois Medical Center, Chicago, IL **Behavioral evidence of the interaction of phencyclidine with catecholamines in primate social colonies.** Federation Proceedings. 35(3):268, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the interaction of phencyclidine (PCP) with catecholamines in primate social colonies was reported. PCP induced slow, repetitive, stereotyped behavior (SB) and increased self-grooming while decreasing social grooming. Chronic administration of d-amphetamine (d-A) induced similar changes in this species. Chronic administration of PCP also induced SB, but ataxia and increased resting were noted. PCP failed to induce hypervigilance at any dose. Since it has been determined that d-A induced SB is modulated by dopamine in this species, the same monkeys were n.g. administered pimozide (PZ), prior to and during chronic PCP treatment. When PZ plus PCP were administered, treated monkeys showed no SB and participated in normal social and solitary activity. Results of these studies indicate that at least some of the behavioral alterations induced by PCP appear to be modulated by catecholamine systems. (Journal abstract modified)

238697 Sepinwall, J.; Sullivan, J. W.; Mitchell, D. N.; Cook, L. Hoffmann-La Roche Inc., Nutley, NJ 07110 **Effects of benzodiazepine antianxiety agents on punished (conflict) and unpunished behavior in drug-naive rats.** Federation Proceedings. 35(3):268, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of benzodiazepine antianxiety agents on punished and unpunished behavior in drug naive rats was reported. In drug naive rats, the predominant effect of either chlordiazepoxide or diazepam was a behaviorally depressant one. However, after three or four single treatments these depressant effects no longer occurred whereas the more typical anticonflict effect was evident. It appears that metabolic induction is not the only factor that may account for the transition from behaviorally depressant activity to anticonflict activity for such agents. At a dose of 10mg/kg p.o.,neither the desmethyl (Ro-5-0883) nor the lactam (Ro-5-2092) metabolites of chlordiazepoxide exhibit initial behaviorally depressant effects in drug naive rats. Either the metabolites do not share this property with the parent compound or a higher dose level of the metabolites may be required to produce this pattern. These metabolities, like chlordiazepoxide or diazepam, do attenuate conflict suppression in drug sophisticated rats. (Journal abstract modified)

238698 McCardle, Katherine; Hirsh, Kenneth. General Foods Corp., Technical Center, Tarrytown, NY 10591 **Reduced spontaneous locomotor activity evoked by L-tryptophan and prevented by D-tryptophan.** Federation Proceedings. 35(3):268, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, reduced spontaneous locomotor activity (SLA) evoked by L-tryptophan and prevented by D-tryptophan (D-Tryp) was reported in mice. The onset of effect was less than 30 minutes and the maximum effect was observed through the first 90 minutes. Thereafter SLA was reduced but the depression was less marked. In another study the influence of D-tryptophan (D-Tryp) by itself and in combination with L-Tryp was investigated. It was found that D-Tryp alone did not alter SLA. When L-Tryp was combined with D-Tryp no depression of SLA was observed. It was concluded that D-Tryp was inactive as a reducer of SLA and that it prevented the action of L-Tryp through an unknown mechanism. In an effort to determine the threshold blocking dose of D-Tryp it was added in varying amounts to a fixed dose of L-Tryp. Doses of D-Tryp below 1g/kg did not interfere with L-Tryp effects. Once again, however, D-Tryp blocked SLA depression evoked by L-Tryp. (Journal abstract modified)

238704 Nozaki, M.; Bell, J. A. NIDA Addiction Research Center, Lexington, KY 40511 **Responses of flexor reflex to LSD, tryptamine (T), 5-HTP, methoxamine (M) and d-amphetamine (A) in acute and chronic spinal rats.** Federation Proceedings. 35(3):270, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, responses of flexor reflex to lysergic acid diethylamide (LSD), tryptamine (T), 5-hydroxytryptamine (5-HTP), methoxamine (M) and d-amphetamine (A) in acute and chronic spinal rats were reported. LSD, T, 5-HTP, M, and A facilitated the flexor reflex and evoked spontaneous hindleg movement in chronic spinal rats. LSD and A were also studied in the acute spinal rat. Increasing dose of LSD to 100microg/kg did not facilitate the flexor reflex, but a dose of 2mg/kg did facilitate this movement. Four but not 2mg/kg of A was facilitatory in the acute spinal rat. The facilitation caused by LSD and T but not 5-HTP in chronic spinal rats was antagonized by cyproheptadine (0.4mg/kg). The facilitatory effects of LSD and T were similar and can be distinguished from 5-HTP. (Journal abstract modified)

238706 Jobe, P. C.; Picchioni, A. L.; Chin, L.; Geiger, P. F. Louisiana State University, School of Medicine, Shreveport, LA 71130 **Effects of Ro 4-1284, iproniazid, methylphenidate, cocaine or imipramine on sound- and pentylenetetrazol-induced seizure in the rat.** Federation Proceedings. 35(3):270, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of imipramine (IM) on pentylenetetrazol (PTZ) seizures and the effects on audiogenic seizure (AGS) of drugs which, although structurally dissimilar to IM, produce an increase of synaptic norepinephrine (NE) levels were reported. It was found that IM exerted essentially the same effect on PTZ seizures as on AGS and that methylphenidate (MP) and cocaine (C) inhibited AGS intensity. Furthermore, the administration of MP, C or iproniazid (IP), in combination with Ro-4-1284, reduced the degree of AGS enhancement produced by Ro-4-1284. In comparison, after pretreatment with alpha-methyl-p-tyrosine (a tyrosine hydroxylase inhibitor), MP and IP were ineffective as antagonists of the Ro-4-1284 enhancement. These findings support the concept that endogenous NE inhibits both PTZ and AGS in rats. (Author abstract modified)

238713 Drawbaugh, Richard; Miksic, Steven; Smith, Nelson; Lal, Harbans. Department of Pharmacology, University of Rhode Island, Kingston, RI 02881 **Naloxone antagonism of conditional reversal of narcotic withdrawal signs and conditional morphine hyperthermia: an indirect evidence for release of endogenous opioid-like substance in the rat.** Federation Proceedings. 35(3):309, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, naloxone antagonism of conditional reversal in narcotic withdrawal signs and condi-

tional morphine hyperthermia were reported in rats. Each morphine injection was paired with a conditional stimulus (CS) provided by an exposure to anise vapors for 30 min. After 35-50 pairings, CS alone was found to produce hyperthermia in nondependent rats and to reverse morphine withdrawal signs (wet shakes, hypothermia, writhing) in the dependent rats. These actions of CS were similar to those produced by narcotic analgesics in both nondependent and dependent rats. In addition, like its antagonism of opiates, naloxone also blocked the above mentioned opioid like actions of CS in a dose dependent manner. Since this antagonism by naloxone was seen in the absence of an exogenously administered narcotic, CS may be considered to cause a release of an endogenous opioid like substance, actions of which are blocked by a narcotic antagonist. (Journal abstract modified)

238717 Libet, Benjamin; Kobayashi, Harou; Tanaka, Tetsuro. Department of Physiology, School of Medicine, University of California, San Francisco, CA 94143 **A dopamine-induced neuronal "memory trace", mediated by cyclic AMP and disruptable by cyclic GMP.** Federation Proceedings. 35(3):326, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a dopamine induced neuronal memory trace mediated by cyclic adenosine monophosphate (cAMP) was reported. The rabbit superior cervical ganglion exhibits a unique heterosynaptic interaction, in which one presynaptic input (releasing dopamine, DA) produces an enduring enhancement (for at least several hours) in a postsynaptic response to another (cholinergic) input. Treatment with dibutyryl cAMP could fully reproduce this modulatory action of DA, in its magnitude and duration, and could occlude the response to any subsequent DA. Evidence indicates that the cAMP action is a direct postsynaptic one, not an indirect one due to a presynaptic release of DA. The retention of the modulatory change, whether induced by DA or cAMP can be disrupted by cyclic guanosine monophosphate (GMP), but only within a limited time period of 10-15 minutes. The DA modulating action provides a model for a disruptable memory storage process which leads to an enduring nondisruptable memory trace, with cAMP mediating the storage reactions. (Journal abstract modified)

238718 Ritter, Sue; Pelzer, Nancy L.; Cox, Colleen M. Washington State University, Pullman, WA 99163 **Protection against stress-induced depletion of brain norepinephrine after prior exposure to chronic stresses.** Federation Proceedings. 35(3):326, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, protection against stress induced depletion of brain norepinephrine (NE) after prior exposure to chronic stress was reported. Analyses reveal that NE depletion after acute footshock and the protection conferred by prior chronic footshock occur in both hypothalamus and forebrain. Protection does not depend on learning to avoid or minimize the footshock. Rats previously shocked while immobilized exhibited no NE depletion when tested unrestrained with high levels of grid shock. Handling also conferred some protection. It is concluded that protection may result from increased synthetic capabilities of NE neurons induced by direct or hormonal means. (Journal abstract modified)

238720 Brown, Judith E.; Kassouny, Margaret E. Florida State University, Tallahassee, FL 32306 **Marijuana induced alterations in feeding behavior and hypothalamic concentrations of norepinephrine and serotonin in the rat.** Federation Proceedings. 35(3):341, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of typical human dose levels of tetrahydrocannabinol (THC) on feeding behavior and hypothalamic concentrations of norepinephrine (NE) and seroronin (5-HT) were reported in rats. Hypothalamic concentrations of NE and 5-HT were determined one and 2 hrs after THC treatment. THC treated rats initially consumed significantly more dry chow and the strongest sucrose solution, consequently more total calories, than controls; however, 24 hr calorie intakes did not differ significantly. Hypothalamic concentrations of NE and 5-HT differed significantly from control values; the direction of the differences depended on THC dose and time after treatment. The results suggest that typical human dose levels of THC produce dose and time dependent effects on food and sucrose intake and hypothalamic NE and 5-HT in rats. (Journal abstract modified)

238722 Fechter, Laurence D.; Annau, Zoltan. Johns Hopkins University, Baltimore, MD 21205 **Effects of chronic prenatal hypoxia on physiological, neurochemical and behavioral development.** Federation Proceedings. 35(3):366, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, evidence that prenatal carbon monoxide (CO) exposure at levels equivalent to or slightly above (12% carboxyhemoglobin) those of heavy cigarette smokers produce similar abnormalities as well as behavioral and neurochemical changes in neonatal rats was presented. Pregnant hooded rats were exposed throughout gestation to either CO or to air until delivery of the litter. The CO neonates had lower birthweights and a significantly reduced growth rate compared to air breathing controls. Cross-fostering studies indicated that this effect was not related to maternal variables during the neonatal period. Activity tests carried out following injection of the catecholamine precursor L-dopa showed lower activity scores among CO subjects between 1 and 14 days of age. Assays for catecholamines showed reduced utilization of L-dopa although monoamine levels did not differ in noninjected controls. Older CO treated rats were also less active than air subjects in tests performed without L-dopa. The results indicate that chronic low level CO exposure during gestation has significant functional effects in neonatal rats. (Journal abstract modified)

238744 Masserano, Joseph M.; King, Carl D. Dept. of Pharmacology, University of Tennessee, Health Science Center, Memphis, TN 38163 **Comparison of thyroid releasing hormone (TRH) and amphetamine (AMP) on changes in activity levels of rats following injections into the caudate nucleus, septum, and hypothalamus.** Federation Proceedings. 35(3):429, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a comparison of thyroid releasing hormone (TRH) and amphetamine (AMP) on changes in activity levels of rats was reported. Cannulae were implanted into the caudate nucleus, septum, and hypothalamus of rats. After recovery from surgery the rats were adapted to photocell monitored Lehigh Valley activity boxes. Three days of control were then obtained, after which intracerebral injections were begun. Saline, TRH, and AMP were injected in a varying sequence into the areas implanted. Results illustrate no change in activity levels from control following saline or AMP injections into any of the areas. TRH caused no change in activity following injections into the caudate nucleus or septum but did cause a significant increase in activity following injections into the hypothalamus. Histological verification confirmed accurate implantations. 2 references. (Journal abstract modified)

238749 McMillan, D. E. Dept. of Pharmacology, School of Dentistry, University of North Carolina, Chapel Hill, NC 27514 **Ethanol, water and food intake under a fixed-interval (FI) schedule of food pellet presentation.** Federation Proceedings. 35(3):467, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study on the effect of ethanol, water and food intake on a fixed-interval (FI) schedule of food pellet presentation in rats was reported. With both water and ethanol solutions (ES) available, the percentages of the total daily fluid intake as ES were about 85%, 40%, and 10%. Subsequently, ES were removed for 4 days. When ES were reintroduced, the percentages of the total daily fluid intake as ES were about 95%, 60%, and 5%. During the first exposure to ES with water freely available, the percentages of the total daily caloric intake as ethanol were about 10%, 6%, and 3%. Upon reexposure to ES after removal for 4 days, the percentages of the total daily caloric intake as ethanol were about 20% and less than 1%. Other rats could lever press for food under the FI schedule only 8 hours a day, with 10% ES as the only fluid for 4 days, followed by 11 days with both water and ES available. These rats obtained fewer food pellets and drank more ES than the rats drinking 10% ES with 24 hour access to the schedule. Ethanol intake was a function of both the concentration of the ES and the availability of food. (Journal abstract modified)

238750 Geller, I.; Messiha, F. S. Southwest Foundation for Research and Education, San Antonio, TX 78284 **Ethanol preference in rats: possible underlying mechanisms.** Federation Proceedings. 35(3):467, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, an evaluation of 2-aminoethylisothiouronium bromide hydrobromide (AET) was presented. Alcohol intake was reduced in rats administered AET in doses ranging from 50-200mg/kg. Daily administrations of 50mg/kg during a 5 day period to nonalcohol drinking rats had no significant effect on liver alcohol dehydrogenase (L-ADH) or liver aldehyde dehydrogenase (L-ALDH). Also studied were noreleagnine (NEG), a beta-carboline previously shown to decrease ethanol drinking in rats and cinanserin (CIN), a 5-hydroxytryptamine (5-HT) receptor blocker previously shown to increase ethanol intake. Daily 50mg/kg doses of CIN during a 5 day period revealed no significant effects on L-ADH or L-ALDH. However, 40mg/kg of NEG given daily over a 5 day period, significantly decreased L-ADH specific activity without a concomitant decrease in L-ALDH activity. (Journal abstract modified)

238754 Mukherjee, B. P.; Pradhan, S. N. Howard University College of Medicine, Washington, DC 20059 **Effects of some psychotropic drugs on aggressive behavior in rats.** Federation Proceedings. 35(3):468, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the effects of several psychotropic agents on three different types of aggressive behavior in rats was reported. Chlorpromazine reduced septal lesion induced hyperexcitability and footshock induced fighting, but had no effect on muricidal activity even at a 5mg/kg dose. Diazepam had little or no effect on septal lesion induced hyperexcitability, but enhanced footshock induced fighting; it also failed to affect the muricidal activity even at 10mg/kg dose. Lithium chloride was found to inhibit septal lesion induced hyperexcitability, but enhanced footshock induced fighting; it also failed to affect the muricidal activity even at a 10mg/kg dose. Lithium chloride was found to inhibit septal lesion induced hyperexcitability and footshock induced fighting to approximately the same extent (up to 30%). Muricidal activity was affected by 127.2mg/kg doses in only 3 out of 10 rats. Repeated administration of lithium chloride significantly inhibited septal lesion induced hyperexcitability and footshock induced fighting, but failed to block muricidal activity. Lithium chloride also antagonized both amphetamine induced facilitation and scopolamine induced suppression of footshock induced fighting. (Journal abstract modified)

238755 Bain, George; Kornetsky, Conan. Boston University School of Medicine, Boston, MA 02118 **The effects of intracranial administration of norepinephrine and intraperitoneal chlorpromazine on attention in the rat.** Federation Proceedings. 25(3):468, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study on the effects of intracranial administration of norepinephrine (NE) and intraperitoneal chlorpromazine (CPZ) on attention in the rat was reported. Systemically administered CPZ attentuated both the impaired performance and the enhanced release of NE resulting from stimulation of the midbrain reticular formation (MRF). To further elucidate the role of NE in this hyperarousal model, push pull cannulae were stereotactically implanted bilaterally in the MRF of the rat. Animals pretreated with CPZ or saline 5 minutes prior to testing on the attention task and then were perfused with NE via one of the push pull cannulae. NE alone caused impairment in performance that was significantly attenuated by pretreatment with CPZ. These results support the hypothesis that the impaired performance seen after electrical stimulation is the result of the release of NE, and that CPZ effects in this model are related to an attenuation of the NE action. (Journal abstract modified)

238756 Krimmer, Edward C.; Barry, Herbert, III. Dept. of Pharmacology, University of Pittsburgh, School of Pharmacy, Pittsburgh, PA 15261 **Discriminative pentobarbital stimulus after intravenous administration: a comparison with the intraperitoneal route.** Federation Proceedings. 35(3):468, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of discriminative pentobarbital stimulus after intravenous administration was reported. The task was to avoid shock scheduled 5 seconds after the animal was placed in the starting compartment by being in the other compartment (active avoidance) following pentobarbital and by being in the starting compartment (passive avoidance) following saline for five animals and the same avoidance responses with the drug conditions reversed for 4 animals. After a preponderence of successful avoidances had been established, tests after other treatments showed that the drug response was elicited by administration of lower doses of pentobarbital and by chlordiazepoxide and alcohol at the same short interval, and by pentobarbital up to 7.5minutes but not at 15 minutes after injection. Subsequent tests and training at longer intervals after intraperitoneal doses of pentobarbital and saline indicated qualitatively similar drug stimulus effects. (Journal abstract modified)

238757 Collier, Timothy J.; Kurtzman, Scott; Routtenberg, Aryeh. Cresap Neuroscience Lab., Northwestern University, Evanston, IL 60201 **Intracranial self-stimulation derived from entorhinal cortex.** Federation Proceedings. 35(3):468, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of intracranial self-stimulation derived from entorhinal cortex was reported. Eighty three adult male albino rats were tested for the reward-

ing properties of brain stimulation in the posterior temporal cortex. Fifteen animals with electrodes directly within or immediately adjacent to the tightly packed cell layer of entorhinal cortex(EC) demonstrated self-stimulation. To assess further the role of dopamine, subjects were additionally studied to determine whether pimozide, the dopamine receptor blocker, would influence self-stimulation. Response rates were reduced to operant levels. Although the response rates in EC are not high, the suggested dopaminergic involvement in self-stimulation and the topographic projection of this structure to hippocampus makes it a suitable structure for further study of the anatomy of brain reward mechanisms. (Journal abstract modified)

238768 Rosecrans, J. A.; Elchisak, M. A.; Schechter, M. D. Dept. of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Dopamine and psychoactive drug action: a further evaluation.** Federation Proceedings. 35(3):506, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, an evaluation of dopamine (DA) and psychoactive drug action was reported. Normal rats and rats chronically depleted of either norepinephrine (NE) or dopamine (DA) were examined. D-amphetamine served as a discriminative stimulus (DS) to operant behavior in NE and DA depleted rats. DA depletion antagonized or facilitated drug induced antinociceptive effects. The DS property of morphine was not affected, but response rate suppression at high doses was significantly reduced by DA depletion. Dose transfer doses of methadone produced similar effects. Stereotypy was not affected by amine depletions. DA depletion did not antagonize d-amphetamine DS effects but did significantly reduce response rate suppression by high doses. NE depletion in antagonized d-amphetamine DS effects but not those of l-amphetamine in transfer studies. (Journal abstract modified)

238781 Schechter, P. J.; Jung, M. J.; Tranier, Y.; Lippert, B.; Sjoerdsma, A. Centre de Recherche Merrell Internationale, Strasbourg, France **Gamma-acetylenic GABA (amino-4-hex-5-ynoic acid): a GABA - transaminase inhibitor with selective anti-seizure activity.** Federation Proceedings. 35(3):544, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the antiseizure activity of gamma-acetylenic gamma-aminobutyric acid (GABA) (amino-4-hex-5-ynoic acid GAG) was reported. GAG protects against audiogenic seizures in susceptible mice with the pattern of protection paralleling the elevation of brain GABA levels. Protection is afforded by doses as low as 5mg every 8 hours which double brain GABA levels. GAG also protects mice against seizures and death induced by thiosemicarbazide, isoniazid, strychnine and electroshock. It has no influence on the incidence of seizures or mortality induced by picrotoxin or pentylenetetrazol even when given at doses which raise GABA four to five times control levels. Hence, GAG appears to possess selective antiseizure activity is some model systems. It is concluded that GAG should be a valuable tool in studies of brain GABA metabolism and its possible relationship to experimentally prodcued seizures. (Journal abstract modified)

238787 Turner, E. G.; Altshuler, H. L. Texas Research Institute of Mental Sciences, Houston, TX 77025 **Conditioned and unconditioned drug effects in a classical conditioning paradigm.** Federation Proceedings. 35(3):563, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the use of a drug state as a conditioned stimulus in a classical conditioning pradigm was reported. Suppression of a single lever operant response served as an index of a classically conditioned response. D-amphetamine injections were paired with a series of unavoidable shocks. Subsequently, the effects of d-amphetamine on operant response totals were compared to effects obtained in control subjects which received unpaired d-amphetamine and shock exposures. D-amphetamine was an effective conditioned stimulus for conditioned suppression of the operant response. Administration of cocaine also produced a decrease in total responses, suggesting stimulus generalization from the shock paired drug to a novel drug. Reduction of external apparatus cues by administering shocks in the operant chamber instead of a separate apparatus produced a more durable suppression effect. Response totals recovered to a maximum of 80% of baseline responding during 12 test sessions. The results suggest that the conditioned suppression paradigm may be a useful tool for investigations of drug stimulus control, providing an alternative to the frequently employed operant discrimination methods. (Journal abstract modified)

238788 Uyeno, Edward T. Stanford Research Institute, Menlo Park, CA 94025 **Effects of methoxylated amphetamines on the maze performance by the rat.** Federation Proceedings. 35(3):563, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the relative potency of hallucinogenic 2,5-dimethoxy-4-methyl amphetamine hydrochloride (DOM) and its ethyl homologue, 2,5-dimethoxy-4-ethyl amphetamine hydrochloride (DOET) in the disruption of a previously learned maze habit of the rat was reported. Initially, male rats of the Wistar strain were trained to swim through an underwater maze without any error during four successive trials. The time of peak effect of DOM and that of DOET on the disruption of the retention performance were 45 min after the intraperitoneal injection. A dose response experiment conducted at the peak time showed that doses of 0.25, 0.5, and 1mg/kg of DOM produced an increase in error scores in a dose related manner. The second dose response study indicated that similar doses of DOET also disrupted the retention performance. The two methoxylated compounds did not differ significantly in potency. However, they were significantly more potent than d-amphetamine hydrochloride and 2,4,5-trimethoxy-amphetamine hydrochloride. (Journal abstract modified)

238794 Balster, Robert L.; Chait, L. D.; King, George W., III. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **The effects of acute and chronic phencyclidine on schedule controlled behavior in the rhesus monkey.** Federation Proceedings. 35(3):564, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effect of acute and chronic phencyclidene (PCP) on schedule controlled behavior in the rhesus monkey was reported. PCP produced a dose related decrease in response rate during both components of the chain schedule. On the last day of chronic administration behavioral observation on ratings of the effects of the 1.0mg/kg dose were taken on three chronic monkeys and on three naive monkeys. A number of measures showed that the chronic animals recovered from anesthesia faster than the naive monkeys. After an 8 day washout period a dose response curve for the acute effects of PCP on schedule controlled responding was obtained as before. In two of the monkeys a four to five fold shift to the right of the postchronic dose response curve occurred. In the third monkey the data were ambiguous since over a wide range of doses there was no apparent shift to the right of the postchronic dose response

curve. These results indicate that significant tolerance development can occur to behavioral effects of PCP. (Journal abstract modified)

238800 Damassa, D. A.; Smith, E. R.; Davidson, J. M. Stanford Univeristy, Physiology Department, Stanford, CA 94305 **A quantitative comparison of relationships between plasma testosterone (T) and two central functions: LH feedback and sex behavior.** Federation Proceedings. 35(3):615, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a quantitative comparison of relationships in rats between plasma testosterone (T) and luteinizing hormone (LH) feedback and sex behavior was reported. Adult male rats, implanted with T filled Silastic capsules at castration were repeatedly bled for T and LH analysis and tested for male sex behavior at frequent intervals. The data indicate that sex behavior is very sensitive to Silastic T, has a very limited DR range and a long response time; whereas LH feedback is less sensitive to T, has a DR range consisting of at least two components and responds with a fairly short latency to changes in the feedback signal.

238804 Ritter, Robert C.; Neville, Marilyn. University of Idaho, Moscow, ID 83843 **Hypothalamic noradrenaline turnover is increased during glucoprivic feeding.** Federation Proceedings. 35(3):642, 1975.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, noradrenaline (NA) and dopamine (DA) disappearance rates in the hypothalami and telencephalons of rats treated with 2-deoxy-D-glucose (2DG) were reported. Forty four male rats were injected with either 2DG or isotonic saline 20 minutes before i.p. injection with alpha-methyl-p-tyrosine (ATM). Food intake of the rats was then monitored to confirm successful induction of glucoprivic feeding. The rats were sacrificed at intervals between 0 and 6 hours after AMT administration. By 2 hours post-AMT hypothalamic levels of 2DG-AMT, treated rats were 30% less than saline AMT treated controls. Telencephalic NA and concentrations of 2DG-AMT treated rats were not distinguishable from those of saline AMT treated rats at any time. The fact that 2DG treatment specifically increased hypothalamic NA turnover reinforces the notion that hypothalamic NA mediates glucoprivic feeding. (Journal abstract modified)

238811 Weiss, Gerald K.; Feeney, Dennis M.; Spiker, Maura. Department of Physiology, University of New Mexico, Albuquerque, NM 87131 **Effect of delta9-THC on physical symptoms and EEG in the naturally epileptic beagle.** Federation Proceedings. 35(3):644, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of delta9-tetrahydrocannabinol (THC) on physical symptoms and electroencephalogram in the epileptic beagle were reported. Myoclonic jerks and generalized seizures were observed only in those dogs receiving high dosages of THC. In six epileptic beagles implanted with cortical and subcortical electrodes, THC reliably evoked myoclonus and temporal lobe seizures. These results indicate that THC, a psychoactive component of marihuana, can activate existing epileptic pathology in beagle dogs. (Journal abstract modified)

238813 Ford, Robert D.; Balster, Robert L.; Beckner, Jacqueline S. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Delta9-tetrahydrocannabinol (delta9-THC) and 11-OH-delta9-THC: onset, pattern and duration of behavioral effects and tolerance in rats.** Federation Proceedings. 35(3):644, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the behavioral effects of delta9-tetrahydrocannabinol (THC) and its 11-hydroxy (11-OH) metabolite in rats maintained on two schedules of food presentation were reported. The onset of 11-OH-THC was faster, varied systematically with dose, and usually abruptly suppressed all responding, while THC's onset was slower, varied little with dose and often resulted in a decreased and steady pattern of responding. 11-OH-THC was about three times as potent, had a shorter duration of effects, and when responding resumed it often returned to control rates within a short time. The return to control responding after THC was prolonged. Tolerance and cross-tolerance developed at the same rate to equipotent doses of the two drugs. Thus, 11-OH-THC differed from THC in onset, potency, pattern and duration of effects while tolerance developed at the same rate. These results are consistent with the hypothesis that 11-OH-THC is responsible for the behavioral effects of THC. (Journal abstract modified)

238814 Harris, R. Adron; Snell, Diane; Loh, H. H.; Leake, Chauncey D. Department of Pharmacology, UCSF, San Francisco, CA 94143 **Effects of hallucinogens on operant behavior.** Federation Proceedings. 35(3):644, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of hallucinogens on operant behavior in rats were reported. The dosages of each drug required to reduce fixed-ratio (FR) responding by 50% were determined for lysergic acid diethylamide (LSD), paramethoxyamphetamine (MPA) 2,4,5-trimethoxy-amphetamine (TMA), 2,4-dimethoxyamphetamine (DMA) 2,4,6-TMA, 2,5-DMA, 2,3,5-TMA 2,3,4-TMA, 3,4-DMA, 2,3,6-TMA, dimethyltryptamine (DMT) and mescaline. All of these drugs also decreased the overall rate of fixed-interval (FI) responding. However, two of the drugs, LSD and PMA, increased the low rates of FI responding occurring at the beginning of the interval, while decreasing the higher response rates occurring at the end of each interval. The other drugs decreased response rates throughout the interval. Thus, in contrast to amphetamine, most of the methoxylated amphetamines, as well as mescaline and DMT, did not display rate dependent effects. The good correlation between the relative potency of these 12 drugs in disrupting rat operant behavior and their potency in producing subjective effects in humans suggests similarities in the mechanisms underlying these two effects. (Journal abstract modified)

238819 York, D. H.; Lentz, S.; Love, G. Department of Physiology, School of Medicine, University of Missouri, Columbia, MO 65201 **Neural discharge associated with tail pinch induced stereotyped behavior.** Federation Proceedings. 35(3):668, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, neural discharge associated with tail pinch induced stereotyped behavior was reported. Chlorpromazine, haloperidol and pimozide all significantly blocked the tail pinch induced response in a double-blind evaluation. Methysergide was ineffective. Single unit discharge was recorded from neurons in the head of the caudate nucleus of lightly anesthetized male rats. Tail pinch was found to markedly depress the discharge of 22 out of 28 spontaneously active cells in the caudate nucleus. This tail pinch induced depression of neuronal discharge was reversible. With repeated testing of the same cell however, the depressant response became less marked. It was antagonized by haloperidol at doses which blocked stereotype behavior. Single unit recordings in the pars compacta and pars reticulata of the

substantia nigra were also undertaken. A preferential increase in cell discharge to tail pinch was observed only from neurons in the pars compacta. These results suggest that tail pinch activates the nigrostriatal dopamine pathway causing depression of neurons in the caudate nucleus. (Journal abstract modified)

238842 Parker, Robert B.; Coughenour, Linda L.; McLean, John R. Parke, Davis & Company, Ann Arbor, MI 48106 **Inhibition of spontaneous and methamphetamine-induced locomotor activity in mice.** Federation Proceedings. 35(3):785, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the inhibition of spontaneous and methamphetamine induced locomotor activity were reported. A series of drugs with a variety of pharmacological effects (chlordiazepoxide, chlorpromazine, clozapine, diazepam, droperidol, haloperidol, pentobarbital, phenobarbital, and thioridazine) were tested as inhibitors of spontaneous and methamphetamine induced locomotor activity. Locomotor activity was measured in mouse actophotometers in the presence of test drug alone or test drug plus a 2mg/kg dose of methamphetamine. The results revealed that for all compounds tested, the same doses produced a 50% inhibition of both spontaneous and methamphetamine induced activity. These results suggest that there may be a common pathway which controls the level of spontaneous and methamphetamine induced locomotor activity, that can be directly or indirectly inhibited by the various drugs tested and that the use of locomotor activity as described cannot be used to differentiate among classes of CNS active drugs. (Journal abstract modified)

238843 Browne, Ronald C.; Segal, David S. University of California, La Jolla, CA 92093 **Environmental influences on the behavioral response to acute and chronic amphetamine administration.** Federation Proceedings. 35(3):785, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of environmental manipulations on the behavioral response to acute and chronic d-amphetamine were reported. Male rats received four daily injections of either saline or 2.5mg/kg d-amphetamine in one of the following environments: housed singly and five per cage; or singly and in groups of 5 within the experimental test chamber. Six hours after the fourth injection all rats were placed in the experimental test chambers and 18 hours later injected with 2.5mg/kg d-amphetamine. The results indicate that the patterns of behavior observed following acute d-amphetamine were markedly influenced by environmental manipulations. The behavioral augmentation was consistently found with chronic d-amphetamine administration independent of the environmental differences between pretest and test conditions. These results were discussed in terms of environmentally dependent alterations in amphetamine disposition and catecholamine biosynthetic capacity. (Journal abstract modified)

238844 MacPhail, Robert C.; Seiden, Lewis S. Department of Pharmacology, University of Chicago, Chicago, IL 60637 **Modulation by response requirements of the effects and interactions of d-amphetamine and alpha-methyl-para-tyrosine on schedule-controlled performance in rats.** Federation Proceedings. 35(3):785, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the modulation of the effects of d-amphetamine (d-A) and alpha-methyl-para-tyrosine (MT) on schedule controlled performance in rats were reported. Under baseline conditions, increasing the fixed-ratio (FR) requirement increased duration of the pause that followed reinforcement and decreased rate of responding. D-A decreased rate of responding in a dose related fashion, with proportionately greater decreases obtained at the larger requirements. Pause duration generally increased with doses of d-A; at the larger requirements, however, decreases in pause were frequently obtained with intermediate doses. Under FR 40 (MT) in doses of 50-1.50mg/kg did not appreciably affect performance, but under FR 180 or FR 240 doses of 25-75mg/kg substantially decreased rate of responding and increased pause duration. Under FR 40, pretreatment with MT enhanced the effects of d-A for two rats; for the other two rats, MT did not modify the effects of d-A on performance. Under FR 180 or FR 240, combinations of MT and d-A almost completely eliminated responding for two rats; for the other two MT attenuated the decreases in responding produced by d-A alone. (Journal abstract modified)

238845 Puri, S. K.; Volicer, L.; Choma, P.; Williams, R.; Pelikan, E. W. Boston University School of Medicine, Boston, MA 02118 **Age-related changes of locomotor activity after amphetamine administration.** Federation Proceedings. 35(3):785, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, age related changes of locomotor activity after amphetamine administration were reported in rats. The effect of aging on cyclic adenosine monophosphate (cAMP) levels, adenylate cyclase (AC) and phosphodiesterase (PDE) activities in the rat striatum was studied. Endogenous cAMP levels were measured by radioimmunoassay after the rats were sacrificed by microwave irradiation. Animals were sacrificed by decapitation for the measurement of AC and PDE activities. Aging did not alter either endogenous cAMP levels or the basal AC activity of the homogenates. In vitro addition of dopamine to homogenates produced a concentration dependent increase in cAMP formation in 4 and 12-month-old rats. However, AC in 24 and 30-month-old rats was insensitive to DA stimulation at all concentrations. Sodium floride (NaF) induced stimulation of AC was not affected by aging. There was however, an age related decrease in PDE activity at low substrate concentrations. Since AC sensitivity to DA was decreased while amphetamine effect was increased with increasing age, it is unlikely that increased sensitivity of striatal DA receptors is responsible for the increased sensitivity to amphetamine induced hyperactivity in aged rats. (Journal abstract modified)

238847 Thut, P. D. Department of Pharmacology, Maryland School of Dentistry, Baltimore, MD 21201 **Effect of Lilly 110140 and methysergid on L-dopa induced changes in locomotor activity (MA) in mice.** Federation Proceedings. 35(3):785, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effect of Lilly 110140 and methysergid on L-dopa induced changes in locomotor activity (MA) in mice were reported. Lilly 110140 pretreatment potentiated the early depressant effects of low doses of L-dopa and reduced the stimulant effects of higher doses of L-dopa. Methysergid, a blocker of 5-hydroxytryptamine (5-HT) receptors, reduced the dose of L-dopa required to produce stimulation of MA and decreased the amount of initial depression of MA produced by L-dopa. The results suggest that 5-HT, released as dopamine (DA) is synthesized from L-dopa, acts to counteract the MA stimulant effects of L-dopa and may be partially causative in producing the depression of MA observed after low L-dopa doses. (Journal abstract modified)

239272 Ellman, Steven J.; Ackermann, Robert F.; Bodnar, Richard J.; Jackler, Frances; Steiner, Solomon S. Dept. of Psychology, Harris Hall, Room 013, City College of New York, 138 St. and Amsterdam Ave., New York, NY 10031 **D- and l-amphetamine differentially mediates self-stimulation in rat dorsal midbrain area.** Physiology & Behavior. 16(1):1-7, 1976.

The effects of d-amphetamine and l-amphetamine on self-stimulation in the rat dorsal midbrain area were investigated. Intracranial self-stimulation (ICSS) response rates elicited from the dorsal noradrenergic bundle were enhanced by d-amphetamine but not by l-amphetamine, suggesting noradrenergic medation. Both isomers equally enhanced ICSS response rates elicited from the midventral periaqueductal area (the oculomotor nuclei, the interstitial nuclei, the dorsal raphe nuclei, and the medial longitudinal fasciculus), suggesting dopaminergic mediation. 39 references. (Author abstract modified)

239275 Nagy, Julia; Decsi, L. Institute of Pharmacology, University Medical School Pecs, 7643 Pecs, P.O. Box 99, Hungary **Effect of some intracerebrally administered drugs on a conditioned reflex in the cat.** Physiology & Behavior. 16(1):21-25, 1976.

The effect of intracerebrally administered drugs on a conditioned reflex in the cat was tested. Injection of carbachol into the anterior hypothalamus or thalamus (intralaminar nuclei) in freely moving cats caused a dose related inhibition of alimentary conditioned reflex performance (CRP). The inhibition directly correlated with the intensity of the emotional (rage) reaction also elicitable by carbachol from these parts of the brain. The inhibition of CRP after intrahypothalamic or intrathalamic carbachol application seemed to be a secondary effect due exclusively to the altered emotional state of the animal. Injection of carbachol into the dorsal or ventral hippocampus as well as the basal or central part of the amygdala also inhibited CRP. This inhibitory effect could only be observed when the electroencephalogram pattern of the animals showed local or propagated seizure discharges. Thus, the inhibition of CRP after intralimbic carbachol application seemed to be a secondary effect due to pathologic alterations in the electrical activity of the brain. All the above effects of carbachol were easily counteracted by topical pretreatment with atropine. Nicotine and noradrenaline were ineffective in all regions investigated. 27 references. (Author abstract)

239284 Burge, Katherine G.; Edwards, David A. Dept. of Psychology, Emory University, Atlanta, GA 30322 **Olfactory bulb removal results in elevated spontaneous locomotor activity in mice.** Physiology & Behavior. 16(1):83-89, 1976.

Bilateral removal of the olfactory bulbs of female Swiss-Webster mice resulted in a striking increase in locomotor activity which remained evident even 2.5months after surgery. The administration of d-amphetamine sulfate resulted in a dose dependent increase in locomotor activity, but bilateral bulbectomy did not potentiate amphetamine's motor stimulant effect. Although the neural processes which mediate bulbectomy induced hyperactivity in the mouse are not known, it is stated that these processes, unlike processes involved in some other lesions which produce hyperactivity, do not interact with the locomotor facilitatory property of d-amphetamine. D-amphetamine sulfate caused a dose dependent decrease in food intake, but there was no interaction between bulbectomy and the anorexic activity of d-amphetamine. The fact that bulbectomized mice display elevated locomotor activity in a non-social situation suggests an effect of bulbectomy upon arousal. It is suggested that many of the previously discovered social behavior deficits produced by bulbectomy are specific manifestations of altered arousal processes. 32 references. (Author abstract)

239290 King, James M.; Cox, Verne C. Dept. of Psychology, University of Texas, Arlington, TX 76019 **Effects of ergocornine and CI-628 on food intake and taste preferences.** Physiology & Behavior. 16(1):111-113, 1976.

The effects of ergocornine and CI-628 on food intake and taste preferences were tested in rats. The prolactin inhibitor, ergocornine, and the estrogen antagonist CI-628 yielded significant food intake suppression and strong taste aversions. It is suggested that the taste aversions obtained may not reflect behaviorally significant toxic effects. The estrogen antagonist yielded food intake effects opposite those observed following ovariectomy. 16 references. (Author abstract)

239523 Turner, Evelyn Grace. University of Houston **Conditioned suppression of an operant response using drugs as conditioned stimuli. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-1253 HC$18.00 MF$7.50 175 p.

The possible use of a drug state as a conditioned stimulus in a classical conditioning paradigm was investigated in four animal experiments. Suppression of an operant response served as an index of a classically conditioned response (conditioned suppression). In all experiments, drug injections were paired with a series of unavoidable shocks. Subsequently, effects of the shock paired drug on operant response rate were compared with those obtained in control Ss receiving unpaired drug/shock experience. Drugs included amphetamine and cocaine, and a saline solution was also used. Results from the four studies suggest that, with further development, the conditioned suppression paradigm may be a useful alternative to operant discrimination in investigating drug stimulus control. Advantages of the paradigm are discussed, concluding that: 1) drug states, as possible representatives of other internal stimuli, may acquire behavioral properties through classical conditioning procedures; and 2) generalization can occur between similar internal stimuli. Results are discussed in the context of possible applications to behavioral problems, such as drug abuse and psychosomatic symptoms. (Journal abstract modified)

239533 Jones, John Michael. University of Tennessee **Drug effects on learning: a two stage drug screen utilizing fixed ratio and serial discrimination reversal learning. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-1955 HC$18.00 MF$7.50 63 p.

The development and analysis of a method for determining drug effects on animal acquisition is described. Amphetamine was initially screened on three different fixed-ratio (FR) schedules to determine behaviorally active dosages. A rate dependent effect was noted that consisted of increased rate as a result of amphetamine administration of FR-4 and decreased rate on FR-8 and FR-12. Results were primarily due to lengthy periods of nonresponding, rather than an effect on terminal response rate. Dosages which were active in the FR situation were then tested in choice and unitary serial discrimination reversal learning. Amphetamine facilitated learning in unitary serial learning by decreasing the number of responses made during S-minus, while it caused deteriorated performance in choice learning due to increased responding to one lever for the majority of Ss tested. Further tests were conducted using chlorpromazine, diazepam, and pentobarbital, but these drugs did not have differential effects due to procedure. High

dosages of chlorpromazine and pentobarbital reduced both S-plus and S-minus responding due to mild sedation, rather than to an effect on learning. Diazepam showed no effect at dosages tested. (Journal abstract modified)

239576 Yaksh, Tony L.; DuChateau, Jim C.; Rudy, Thomas A. School of Pharmacy, University of Wisconsin, Madison, WI 53716 **Antagonism by methysergid and cinanserin of the antinociceptive action of morphine administered into the periaqueductal gray.** Brain Research (Amsterdam). 104(2):367-372, 1976.

Methysergid and cinanserin were administered to rats to determine whether the blockade of activity of serotonergic synapses in the central nervous system would antagonize the antinociceptive action of microinjected morphine acting locally within the periaqueductal gray (PAG). Following antagonism by i.p. injection of these agents, a statistically significant reversal of the antinociceptive action of morphine on the tail flick was obtained. In contrast, in control experiments, the antagonists alone appeared to have little effect on tail flick latency, and microinjection of methysergide at the same site as the microinjection of morphine caused no observable reduction in tail flick latency. Results emphasize the relative importance of the PAG in mediating the action of morphine in the production of behaviorally defined antinociception, but the location of the relevant synapse or synapses sensitive to these antagonists was not determined. 33 references.

239673 Barraco, Robin A.; Stettner, Laurence J. Dept. of Physiology, Wayne State Univ. School of Medicine, 540 E. Canfield Ave., Detroit, MI 48201 **Antibiotics and memory.** Psychological Bulletin. 83(2):242-302, 1976.

Investigations of antibiotics as potential amnesic agents in different species using a variety of learning paradigms are reviewed. It is noted that the major classes of antibiotics used to investigate effects on protein synthesis have different mechanisms and different amnesic effects. Close examination of the literature indicates that all of these antibiotics have side-effects but that sufficient control procedures have been used in a variety of experiments to justify an amnesic interpretation of antibiotic induced deficits on retention tests. The data further suggest that antibiotic induced amnesia is generally reversible by chemical or behavioral means. An intensive review of the studies relevant to the neurochemical effects of the major antibiotics suggests that protein synthesis per se is not the crucial correlate of their behavioral effects and that there are probably different modes of chemical action corresponding to the different behavioral effects. Several possible mechanisms are discussed in detail, most notably glutarimide effects on neurotransmitter activity and the relationship of puromycin to brain peptides. 240 references. (Author abstract modified)

239826 Gianutsos, Gerald; Harbans, Lal. Dept. of Pharmacology, Michigan State Univ., East Lansing, MI 48823 **Alteration in the action of cholinergic and anticholinergic drugs after chronic haloperidol: indirect evidence for cholinergic hyposensitivity.** Life Sciences (Oxford). 18(5):515-520, 1976.

Indirect evidence for cholinergic hyposensitivity in rats was found in a study of alteration in the action of cholinergic and anticholinergic drugs after chronic haloperidol treatment. Following repeated treatment with haloperidol, spontaneous locomotor activity and the locomotor stimulation produced by amphetamine and the anticholinergic dexetimide was enhanced compared with normal rats. The reduction in locomotor activity produced by the cholinergic agonist pilocarpine was retarded following this treatment. These results suggest that a dopaminergic supersensitivity and a cholinergic hyposensitivity develop as a result of chronic neuroleptic treatment. 39 references. (Author abstract modified)

239829 Vergnes, Marguerite; Penot, Christine. Lab. de Neurophysiologie, Centre de Neurochimie du CNRS, Rue Humann 11, 67000 Strasbourg, France /**Intraspecies aggression induced by electrical shock and reactivity after raphe lesions in the rat. Effects of physostigmine.**/ Agression intraspecifique induite par chocs electriques et reactivite apres lesion du raphe chez le rat. Effets de la physostigmine. Brain Research (Amsterdam). 104(1):107-119, 1976.

Shock induced fighting behavior, flinch/jump thresholds and locomotor open-field activity were studied following dorsal and medial raphe lesions in rats. Attack scores were raised for low intensity shocks (1 mA) only, whereas they remained unchanged for shocks of higher intensity (2 mA), as compared to controls. The jump threshold was decreased in raphe lesioned animals, but the flinch threshold was unchanged. Physostigmine reduced the lesion induced hypereactivity: locomotor open-field activity was reduced to a greater extent than in the controls, and habituation to the open-field situation was restored. Doses of physostigmine that did not modify shock induced aggression in controls reduced aggression in lesioned animals to the level shown by controls for low intensity shocks. In conclusion, shock induced aggression is not directly dependent on a serotonergic brain mechanism. The behavioral changes observed are related to the hyperreactivity induced by raphe lesions. This hyperreactivity presumably results from a reduced activity of cholinergic brain mechanisms. 47 references. (Journal abstract)

239834 Nitsch, F.; Hassler, R.; Kim, J. S.; Bak, I. J. Deutschordenstrasse 46, 6000 Frankfurt/M. 71, Germany /**The anxiolytic effect of small cumulative doses of oxypertin in rats in an anxiety test and the possible neurochemical correlates in the hypothalamus and striatum.**/ Uber die anxiolytische Wirkung von kleinen cumulativen Dosen von Oxypertin auf Ratten um Angsttest und ihre moglichen neurochemischen Korrelate im Hypothalamus und Striatum. Nervenarzt (Berlin). 47(1):40-45, 1976.

Ten rats in an anxiety experiment were given oxypertin twice daily. The average hesitation time of the treated rats was reduced between 7.4and 2.6seconds. The anxiolytic effect was accompanied by an approximately 20% reduction in serotonin concentration in the hypothalamus, and a parallel 12% reduction in noradrenaline levels. It is suggested that this may indicate increased turnover of these substances in the hypothalamus. In addition, the link of this oxygpertin induced lowering of noradrenaline and serotonin levels to the ascending noradrenergic system from the locus coeruleus is discussed. 45 references.

239841 Crow, T. J.; Wendlandt, S. National Institute for Medical Research, Mill Hill, London NW7 1AA, England **Impaired acquisition of a passive avoidance response after lesions induced in the locus coeruleus by 6-OH-dopamine.** Nature (London). 259(5538):42-44, 1976.

The hypothesis that the integrity of the coerulo/cortical noradrenergic pathway is necessary for avoidance learning was investigated in 79 female Sprague-Dawley rats. Animals were divided into four groups: untreated control; sham lesion control; bilateral lesion of the locus coeruleus with 6-hydroxydopamine (6-OHDA); and treatment with diethyldithiocarbamate (DDC), a dopamine-beta-decarboxylase inhibitor. Both 6-

OHDA and DDC treated rats showed normal immediate acquisition of the avoidance response but showed a failure of retention after 3 days, as compared to the control groups. Since immediate acquisition was unimpaired, it is concluded that it is unlikely that the deficit is due to impaired sensory or motor capacity; more probably it represents a defect in the capacity to form a long-lasting record of previous experience. Results are compatible with the hypothesis that the integrity of noradrenergic neurons ascending from the locus coeruleus is necessary for initiating the transition from a short-term to a long-term memory trace. 15 references.

239848 Otero, Jesus B.; Mirsky, Allan F. Lab of Neurophysiology, NIMH, Bethesda, MD 20014 **Influence of secobarbital and chlorpromazine on precentral neuron activity during attentive behavior in monkeys.** Psychopharmacologia (Berlin). 46(1):1-9, 1976.

Precentral motor cortex neurons were studied under nondrug and drug conditions in three trained monkeys during the performance of a go/no go visual attention task. The two drugs studied, secobarbital and chlorpromazine, produced differing patterns of effect on components of the motor sequence involved in reaction time. The following components were considered: the stimulus firing (SF) interval; the firing response (FR) interval; and movement time (MT). Secobarbital produced an increase of 80% in SF and a relatively small average change in FR although there was considerable variability in the latter. MT was decreased in most secobarbital experiments. Anatomical factors relating to the FR variability were considered, and the MT decrease was discussed in terms of possible excitatory effects of the drug. Chlorpromazine produced small increases in SF, FR and MT, alternating with periods of complete abolition of performance. The results were discussed in terms of theories of attention deficit following administration of secobarbital and chlorpromazine. 12 references. (Author abstract modified)

239850 Leith, Nancy J.; Barrett, Robert J. Tennessee Neuropsychiatric Inst., Central State Hospital, 1501 Murfreesboro Rd., Nashville, TN 37217 **Amphetamine and the reward system: evidence for tolerance and post-drug depression.** Psychopharmacologia (Berlin). 46(1):19-25, 1976.

A study which shows that physiological tolerance develops to the facilitation of self-stimulation behavior which d-amphetamine produces is presented. Rats were trained to barpress for electrical stimulation of the medial forebrain bundle and tested for facilitation of responding following the administration of 0.25 or 0.50 mg/kg d-amphetamine. Testing was terminated for 4 days during which increasing doses (1.0-12.0mg/kg) of the drug were given. Sixteen hours after the last injection, the test doses (0.25 or 0.50 mg/kg) no longer produced facilitation of self-stimulation. In addition, testing on the following day with no further administration showed a depression of responding indicating depression of the sensitivity of the reward system of the brain. 26 references. (Author abstract modified)

239852 Riege, Walter H.; Cherkin, Arthur. Psychobiology Research Lab, VA Hospital, Sepulveda, CA 91343 **Memory performance after flurothyl treatment in rainbow trout.** Psychopharmacologia (Berlin). 46(1):31-35, 1976.

Fingering rainbow trout (N=436) were trained in one trial with brief electric shock (2.0V/cm) to suppress their spontaneous upstream swimming into a quiet well. Memory retention one day later was not influenced by the temperature at which they had been acclimated, trained and tested (10 degrees C, 15 degrees C or 20 degrees C). When exposed 4 min after training for 2 min, to a flurothyl solution (10, 25, 50, 100 or 200 microliters 1) trout convulsed and overturned. The onset of overturn was concentration and temperature dependent. Flurothyl altered the one day retention of avoidance behavior; low concentrations enhanced, whereas high concentrations impaired. Memory enhancing low concentrations of flurothyl, applied after posttraining amnesic treatment with carbon dioxide, reversed the carbon dioxide amnesia. 33 references. (Author abstract)

239856 Jones, Catherine N.; Grant, Lester D.; Vospalek, Dawn M. 229 Biological Sciences Research Ctr. of the Child Devel. Inst., Div. of Health Affairs, Univ. of North Carolina, Chapel Hill, NC 27514 **Temporal parameters of d-amphetamine as a discriminative stimulus in the rat.** Psychopharmacologia (Berlin). 46(1):59-64, 1976.

Three groups of rats were trained on a two level operant discrimination task using d-amphetamine (0.8, 1.6or 2.4mg/kg) and saline as cues. Reinforcement of responding on one lever was associated with the drug and reinforcement on the other level was associated with saline. Following acquisition, behavioral control was evaluated during 10 min extinction tests at 0, 15, 30, 60, 90, 120, 180, or 240 min after injection of drug or saline. Onset of the stimulus properties of d-amphetamine occurred within 10 min and maximal effects were attained by 15-30 min postinjection. Drug effects were minimal or absent 2-4 hr after administration. The time course for all doses of d-amphetamine was identical when each group was tested with its respective training dose. When subjects were tested with doses other than their training dose, the time course of the drug effect varied as a function of training dose, test dose and time after injection. 36 references. (Author abstract)

239857 Ts'o, Timothy O. T.; Hance, A. J.; Killam, Keith F. Univ. Psychiatric Service, SUNY, Bldg. L-4, Central Islip Psychiatric Ctr., Central Islip, NY 11722 **Performance enhancement effects of d-amphetamine, methylphenidate, pipradrol and phenindamine in rats.** Psychopharmacologia (Berlin). 46(1):65-72, 1976.

A multiple behavioral schedule with food reinforcement was designed to measure the drug induced performance enhancement and noneffective activity in rats. The 20min schedule had continuous reinforcement schedule components in the 33 trials and extinction components in the intertrial periods. During each trial, food reinforcement was present in the limited period, which was preceded by a discriminative stimulus (either a light or a footshock). The rats generated a high rate of lever pressing during the limited period and a low rate of lever pressing during the intertrial period. The drugs studied were d-amphetamine, methylphenidate, pipradrol and phenindamine. At low dosages these drugs increased further the high rate of lever pressing (performance enhancement effect). At higher doses, the drugs increased the low rate of lever pressing, decreased the high rate of lever pressing, and decreased responding of the rats to the discriminative stimulus. This latter pattern was considered to be the noneffective activity caused by the drugs. As expected, d-amphetamine was the most potent. Minor differences in drug effects were seen between the group of rats having light and the group having footshock as discriminative stimulus. 21 references. (Author abstract modified)

239860 Bergmann, Felix; Chaimovitz, Moshe; Pasternak, Varda. Dept. of Pharmacology, Hebrew Univ.-Hadassah Medical School, Jerusalem, Israel **Dual action of morphine and re-**

lated drugs on compulsive gnawing of rats. Psychopharmacologia (Berlin). 46(1):87-91, 1976.

Rats received daily i.p. injections of p-chlorophenylalanine (PCPA) for 3 days, before morphine and related drugs were implanted into the lateral thalamus or injected systemically. PCPA enhanced the stereotyped response to morphine, methadone, and apomorphine, as expressed by compulsive gnawing, but abolished the antagonistic effect of large doses of i.p. morphine. Thus, suppression of gnawing by large doses of systemic morphine and related analgesics may be mediated by a serotoninergic pathway. PCPA also brought to light the ability of pethidine to cause gnawing, which is otherwise suppressed by the strong antagonistic effect of this drug. Morphine and related analgesic drugs exert a dual effect: stimulation of gnawing via a catecholaminergic mechanism and inhibition of gnawing by a serotoninergic mechanism. 12 references. (Author abstract)

239861 Buresova, O.; Bures, J. Institute of Physiology, Czechoslovak Academy of Sciences, Prague, Czechoslovakia **Piracetam-induced facilitation of interhemispheric transfer of visual information in rats.** Psychopharmacologia (Berlin). 46(1):93-102, 1976.

The effect of Piracetam on learning mediated by transcommissural information flow was studied in hooded rats. Acquisition of monocular pattern discrimination was faster in drug treated rats than in untreated controls. Subsequent relearning with one hemisphere functionally eliminated by cortical spreading depression showed that the strength of the primary engram formed under Piracetam in the hemisphere contralateral to the trained eye remained unaffected but that the secondary trace (in the ipsilateral hemisphere) was considerably improved and almost equalled the primary one. Learning with uncrossed optic fibers was unaffected by the drug. Interhemispheric transfer of lateralized visual engrams acquired during functional hemidecortication was facilitated by Piracetam administration preceding the five transfer trials performed with the untrained eye open. Piracetam was ineffective when the trained eye was open during transfer trials. After a visual engram had been lateralized by 5 days of monocular overtraining, Piracetam faciliated formation of the secondary engram induced by three interocular transfer trials. It is concluded that Piracetam enhances transcommissural encoding mechanism activated in the initial stage of monocular learning and in some forms of interhemispheric transfer, but does not affect the transcommissural readout. 33 references. (Author abstract modified)

239863 Schreiber, Henry L.; Wood, W. Gibson; Carlson, Richard H. Dept. of Psychology, Texas Tech Univ., P. O. Box 4100, Lubbock, TX 79409 **Tolerance in methylphenidate-induced locomotion in prairie dogs (Cynomys ludovicianus).** Psychopharmacologia (Berlin). 46(1):111-113, 1976.

The theory that no tolerance develops in methylphenidate-induced activity of rodents was examined, using prairie dogs (Cynomys ludovicianus). After a 5-day adaptation period in activity wheels, four prairie dogs were assigned to a methylphenidate group and four prairie dogs were assigned to a saline group for ten consecutive daily injections. Half revolutions of locomotor activity were recorded during seven measurement periods taken daily. During the third measurement period, from 1-3 hrs following injection, the methylphenidate group declined in locomotor activity over the first 3 days of drug administration. Results indicate that tolerance developed in the methylphenidate induced activity of prairie dogs. 7 references. (Author abstract modified)

239865 Driscoll, P. Vet. -Physiol. Inst., Univ. Zurich, Winterthurerstrasse 260, CH-8057, Zurich, Switzerland **Nicotine-like behavioral effect after small dose of mecamylamine in Roman High-Avoidance rats.** Psychopharmacologia (Berlin). 46(1):119-121, 1976.

Nicotine and mecamylamine were compared in a shuttle box test with rats, in which a dose related, stimulant effect of nicotine had previously been demonstrated. Ten naive, 7-month-old female Roman High-Avoidance (RHA) rats were trained to perform an avoidance task to a high level of efficiency. All injections were subcutaneously administered 30 min before the first runs. Each rat was tested on all 5 testing days of each of the three sessions: 1) a continuation of the training procedure, consisting of 15 runs with a conditioned stimulus - unconditioned stimulus interval of 6 sec; 2) 10 runs each in the shuttle box under extinction procedure conditions; 3) a duplication of the second session. The dose related stimulant effect of nicotine, producing shorter response latencies than those of the control condition, agreed with results of the earlier extinction procedure study. Smaller doses of mecamylamine (25mg/kg) stimulated the rats to the same degree as did 0.1mg/kg nicotine. It is concluded that mecamylamine may exert unpredictable effects on rats at the dosage levels used to block nicotine in behavioral test, a factor to be considered when test results are interpreted. 10 references.

239958 Messing, Rita B.; Phebus, L; Fisher, Laurel A.; Lytle, L. D. Dept. of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **Effects of p-chloroamphetamine on locomotor activity and brain 5-hydroxyindoles.** Neuropharmacology (Oxford). 15(2):157-163, 1976.

The effects of p-chloroamphetamine on locomotor activity and brain 5-hydroxyindoles were examined in rats. p-Chloroamphetamine increased locomotor activity in rats for up to 3 days following a single injection; the peak increase in drug induced activity occurred on the second day. Spinal cord and brain regional concentrations of 5-hydroxytryptamine and 5-hydroxyindoleacetic acid were reduced within 2 days after administration of p-chloroamphetamine, with the greatest reductions occurring in forebrain areas. Brain 5-hydroxyindoles were still reduced in all areas except the midbrain and spinal cord for as long as 1 week after drug treatment. The effects of p-chloroamphetamine on both locomotor activity and brain 5-hydroxytyptamine were blocked by pretreatment with Lilly-110140, a selective uptake inhibitor in brain serotonin neurons. Results suggest that brain serotonin neurons may normally inhibit locomotor activity and that p-chloroamphetamine destroys this inhibitory system. The basal levels of activity return to normal even though brain serotonin is reduced chronically. The possible reasons for these effects are discussed. 30 references. (Author abstract)

239964 Costall, B.; Naylor, R. J.; Pinder, R. M. Postgraduate School of Studies in Pharmacology, Univ. of Bradford, Bradford, West Yorkshire, England **Mechanisms of a dyskinesia induction by 1-(3,4-dihydroxyphenyl)piperazine in the rat.** Neuropharmacology (Oxford). 15(3):203-210, 1976.

Mechanisms of dyskinesia induction by 1-(3,4-dihydroxyphenyl) piperazine were examined in the rat. The unilateral intrastriatal (caudate putamen) administration of 1-(3,4-dihydroxyphenyl) piperazine in the rat induced abnormal involuntary movements. Identical effects were observed after injections into the globus pallidus (after larger doses and delayed onset), tuberculum olfactorium (delayed onset), nucleus accumbens septi, hippocampus and cerebral cortex, but typical abnormal involuntary movements were not observed after in-

jections into the thalamus, midbrain reticular formation and substantia nigra. From a large number of phenylpiperazine derivatives tested, only 1-(3-hydroxyphenyl) piperazine induced abnormal involuntary movements but the effect was less than that of 1-(3,4-dihydroxyphenyl) piperazine. However, intrastriatal picrotoxin, (+)-tubocurarine and carbachol induced effects identical to those of 1-(3,4-dihydroxyphenyl) piperazine. Complete inhibition of the abnormal involuntary movements was achieved by the intrastriatal administration of gamma-aminobutyric acid and sodium valproate. Sodium valproate was also effective by peripheral administration. In addition, unilateral intrastriatal serotonin abolished the 1-(3,4-dihydroxyphenyl) piperazine effects. Results indicate modulatory effects of gamma-aminobutyric acid and serotonin on the activity of the dopamine containing striatum in the control of motor function. 25 references. (Author abstract)

239978 Trulson, M. E. Dept. of Psychology, Princeton University, Princeton, NJ 08540 **Role of superior colliculus serotonin in the grooming behaviour of cats.** Neuropharmacology (Oxford). 15(2):91-97, 1976.

Evidence is provided that a serotonergic system in the superior colliculus is involved in the regulation of grooming behavior in the cat. Significant decreases in tryptophan hydroxylase activity and serotonin content were found in the superior colliculi of cats with pontile lesions and frontal neocortical lesions, which display a dissociation of appetitive and consummatory grooming behaviors. Neither tryptophan hydroxylase activity nor serotonin content were significantly changed in thyroidectomized cats which display the same abnormal grooming behavior. 5-Hydroxytryptophan administration or monoamine oxidase inhibition plus tryptophan administration abolished the abnormal grooming behavior in each of the three groups of cats, suggesting that the change in a serotonergic system is a critical aspect of the abnormal behavior in cats with pontile lesions and frontal neocortical lesions and that a serotonergic system may also be involved in the genesis of the abnormal grooming behavior in thyroidectomized cats. Functional inactivation of the serotonergic system by lysergic acid diethylamide administration or by serotonin receptor blockade did not induce the abnormal grooming behavior in normal cats, indicating that other factors, possibly glucocorticoids, are involved in the genesis of the abnormal behavior. It is concluded that a serotonergic system in the superior colliculi, operating at some level of glucocorticoid function, is involved in the integration of appetitive and consummatory grooming behaviors. 27 references. (Author abstract modified)

239979 Ts'o, T. O. T.; Chenoweth, M. B. Dept. of Psychiatry, State University of New York, Stony Brook, NY 11794 **Comparison between chronic chlordiazepoxide treatment and shock removal in a conflict situation in rats.** Neuropharmacology (Oxford). 15(2):99-101, 1976.

The different psychopharmacological actions of chlordiazepoxide in rats were analyzed using a conflict schedule and chronic administration of the drug. The effects of footshock removal and drug treatment were compared. Individual variance in the rat population was also examined. The 20 min schedule consisted of alternating 5 min periods of fixed-ratio 10 and continuous reinforcement plus shock schedules, which is a conflict situation. Chronic treatment with chlordiazepoxide and with footshock removal significantly increased response rate during the conflict situation. Shock removal produced a much higher rate of response. Individual rates of responding were much less varied during the shock removal period than during the period with a fixed level of footshock. Animals which were less depressed by footshocks showed a higher rate of responding with chlordiazepoxide treatment. Qualitative differences between chlordiazepoxide and shock removal treatment revealed the well established anti-anxiety properties and effects which increase lever pressing rates. 15 references. (Author abstract)

239980 Olds, M. E.; Gardner, M. Div. of Biology, California Institute of Technology, Pasadena, CA 91125 **Effects of diazepam and phenobarbital on self-stimulation in posterior hypothalamic and preoptic regions and on the thermoregulatory responses to rewarding brain stimulation.** Neuropharmacology (Oxford). 15(2):103-115, 1976.

The effects of diazepam and phenobarbital on body temperature changes induced by self-stimulation behavior were investigated in rats. After 10 and 15 min of self-stimulation, the body temperature of the subjects responding for stimulation rose. The rate of responding and the amount of total brain stimulation taken during this period was higher for the group rewarded with hypothalamic stimulation than for the preoptic group, but the duration of the stimulus trains was greater for the preoptic group than for the hypothalamic. In control subjects, diazepam and phenobarbital at the low dose increased the body temperature and at the high dose decreased it. In both groups of self-stimulators, the drugs at the low dose failed to potentiate the increases in body temperature induced by self-stimulation behavior itself, although the drugs increased the rate of self-stimulation or the total time with brain stimulation or the mean duration of the stimulus trains. At the high dose, both drugs caused the increases in body temperature induced by hypothalamic self-stimulation behavior to be smaller. At the high dose, diazepam blocked the increase in body temperature by preoptic self-stimulation behavior. Phenobarbital was not similarly effective during preoptic self-stimulation. At the time of these effects on body temperature the total amount of brain stimulation received during the sessions and the duration of the stimulus trains increased. The findings indicate a dissociation between the effects of diazepam on body temperature and on self-stimulation behavior when reward was in the preoptic region, but not when reward was in the posterior lateral hypothalamic region. 17 references. (Author abstract modified)

239981 Olds, M. E. Div. of Biology, California Inst. of Technology, Pasadena, CA 91125 **Effectiveness of morphine and ineffectiveness of diazepam and phenobarbital on the motivational properties of hypothalamic self-stimulation behaviour.** Neuropharmacology (Oxford). 15(2):117-131, 1976.

The actions of diazepam, phenobarbital, and morphine on self-stimulation were investigated to find out whether the site of action of these drugs is in the reward pathway when facilitation or suppression of responding for brain stimulation is observed. A self-stimulation test at a given intensity of stimulation was always initiated with priming stimuli. It was found that self-stimulation responses were dose dependent for all three drugs. Responding for brain reward was maintained with only minor reductions in rates when the tests were initiated with priming stimuli. Tests to determine the time course of the drugs showed that the time of peak action was between 30-45 min after injection, the time when brain stimulation counteracted the sedation produced by diazepam and phenobarbital. The minor effects of diazepam and phenobarbital at high doses were not due to the development of tolerance because similar effects were obtained in subjects not previously treated with the drugs. The main finding was the

absence of a strong depressant effect on the rate of self-stimulation after large doses of diazepam and phenobarbital, but the presence of depressant effects on the rate of responding after small doses of morphine. These results indicate the possibilty that the first two compounds, at doses that sedate, have minor effects on the motivational properties of hypothalamic stimulation while morphine, at doses that sedate, has major effects on these properties. 13 references. (Author abstract modified)

240009 Morse, W. H. Laboratory of Psychobiology, Dept. of Psychiatry, Harvard Medical School, Boston, MA **Introduction: the control of behavior by consequent drug injections.** Pharmacological Reviews. 27(3):301-305, 1975.

The experimental use of drugs as behavioral reinforcers is discussed, with emphasis on the increased use of various injection schedules as a means of developing and extending models of learned behavior. The changing attitude of the scientific community toward engendering stable, schedule controlled behavior with consequent drug injections is considered. The application of experimental findings to problems of human drug abuse is analyzed in terms of the relation of sequential, temporal contingencies to behavior. 10 references.

240010 Kelleher, R. T. Laboratory of Psychobiology, Dept. of Psychiatry, Harvard Medical School, Boston, MA **Characteristics of behavior controlled by scheduled injections of drugs.** Pharmacological Reviews. 27(3):307-323, 1975.

The literature on reinforcement of behavior in experimental animals through injections of various classes of drugs is reviewed. The importance of the schedule of drug injections in determining how drugs function as reinforcers is stressed. The technique provided by certain second order schedules for establishing powerful control over behavior with drugs such as cocaine, methohexital, and morphine is discussed. 37 references. (Author abstract modified)

240011 Goldberg, S. R. Laboratory of Psychobiology, Dept. of Psychiatry, Harvard Medical School, Boston, MA **Stimuli associated with drug injections as events that control behavior.** Pharmacological Reviews. 27(3):325-340, 1975.

Experimental studies that illustrate the different ways in which behavior can be modified and controlled by environmental stimuli associated with drug injection are reviewed. Stimuli associated with the morphine withdrawal syndrome, with narcotic antagonist injections, and with morphine injection are considered. Various approaches to the experimental analysis of the control of behavior by such stimuli are discussed. 38 references.

240012 Kelleher, R. T.; Goldberg, S. R. Laboratory of Psychobiology, Harvard Medical School, Boston, MA **Introduction: complex schedules of drug injection.** Pharmacological Reviews. 27(3):341-342, 1975.

Procedures for maintaining alternative responses in behavioral control studies are discussed. The most important characteristics of these types of complex schedules are illustrated through a review of some studies in the literature. The use of relative response measures is considered to be a potential advantage of complex schedules involving alternative responses. 7 references.

240013 Johanson, Chris E. Dept. of Psychiatry, Pritzker School of Medicine, University of Chicago, Chicago, IL **Pharmacological and environmental variables affecting drug preference in rhesus monkeys.** Pharmacological Reviews. 27(3):343-355, 1975.

A series of experiments on the effects of several pharmacological and environmental variables on drug preference in rhesus monkeys self-injecting psychomotor stimulant drugs is reported. Preference was determined in a choice procedure which limited drug intake, and a rate free measure of preference was used. Comparative dose preferences among cocaine, methylphenidate, and diethylpropion are presented, and factors modifying drug preferences are described. 37 references.

240014 Griffiths, Roland R.; Wurster, Richard M.; Brady, Joseph V. Div. of Behavioral Biology, Dept. of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD **Discrete-trial choice procedure: effects of naloxone and methadone on choice between food and heroin.** Pharmacological Reviews. 27(3):357-365, 1975.

The use of the choice procedure with male baboons (Papio anubis) to examine the effect of the narcotic antagonist naloxone and the opiate methadone on the choice between heroin and food reinforcers, is reported. The results indicate that naloxone produces dose related increases in selection of heroin over food, while methadone produces decreases in this same measure. The difficulty of explaining the findings in terms of behavioral mechanisms is discussed. 17 references.

240015 Iglauer, Carol; Llewellyn, Mark E.; Woods, James H. Veterans Administration Hospital, Lexington, KY 40507 **Concurrent schedules of cocaine injection in rhesus monkeys: dose variations under independent and non-independent variable-interval procedures.** Pharmacological Reviews. 27(3):367-383, 1975.

The responses of rhesus monkeys (Macaca Mulatta) under concurrent schedules of intravenous cocaine injection were examined. Results indicate support for the contention that if comparable conditions can be created, schedule controlled behavior maintained by cocaine injections will be comparable to schedule controlled behavior maintained by other reinforcers. When compared with findings from concurrent schedule studies with other reinforcers, the data are strikingly similar with respect to the preferences exhibited for higher reinforcement parameters and the matching shown to relative obtained reinforcement. 36 references.

240016 Catania, A. Charles. Dept. of Psychology, University of Maryland Baltimore County, 5401 Wilkens Avenue, Baltimore, MD 21228 **Drug effects and concurrent performances.** Pharmacological Reviews. 27(3):385-394, 1975.

The importance of examining drug effects for their potential relevance to the analysis of behavior is discussed. The various ways in which drug studies can contribute to an understanding of behavior are elucidated against the background of a review of studies in the literature. Comparison of food and drugs as reinforcers, absolute and relative measures of reinforcer potency, and the fallibility of the matching law are considered. 21 references.

240017 Goldberg, S. R.; Kelleher, R. T. Laboratory of Psychobiology, Dept. of Psychiatry, Harvard Medical School, Boston, MA **Introduction: schedules of termination of drug injections.** Pharmacological Reviews. 27(3):395-396, 1975.

Schedule controlled patterns of responding which can be maintained in experimental animals by injections of various drugs abused by humans are discussed, and relevant literature is reviewed. It is noted that the techniques that have been used to study behavior maintained by termination of stimuli

associated with drug injections are modifications of techniques originally developed by experimental psychologists to study the behavioral effects of electric shocks. Disparate effects observed using both these experimental models are considered. 17 references.

240018 Downs, David A.; Woods, James H. Dept. of Pharmacology, University of Michigan, Ann Arbor, MI 48104 **Naloxone as a negative reinforcer in rhesus monkeys: effects of dose, schedule, and narcotic regimen.** Pharmacological Reviews. 27(3):397-406, 1975.

Rhesus monkeys (Macaca Mulatta) were used in a series of experiments investigating the effects of naloxone under fixed-ratio, fixed-interval, and continuous avoidance escape schedules. Experimental variables affecting behavior maintained by the termination of naloxone infusions, by the termination of stimuli that preceded naloxone infusions, or by naloxone presentation are described. The behavioral outcome of naloxone administration is shown to depend on the temporal and conditional relationships of naloxone injection to behavior (schedule contingencies), physical dimensions of the stimulus (dose), and antecedent behavior or pharmacological conditions (previous training or exposure to narcotics). 23 references.

240019 Tang, Andrew H.; Morse, W. H. Upjohn Company, Kalamazoo, MI **Termination of a schedule complex associated with intravenous injections of nalorphine in morphine-dependent rhesus monkeys.** Pharmacological Reviews. 27(3):407-417, 1975.

The maintenance of behavior by stimulus nalorphine termination was examined in the morphine dependent and postdependent rhesus monkey responding under fixed-ratio schedules. Variations of the basic schedules for termination of a stimulus associated with nalorphine injections were employed. The results are discussed in terms of the acquisition of behavior and performance under a three response fixed-ratio schedule during morphine dependence and withdrawal and under a 30 response fixed-ratio schedule under the same conditions, as well as the termination of a stimulus light associated with intravenous injections of different doses of nalorphine. 13 references.

240020 Hoffmeister, Friedrich; Wuttke, Wolfgang. Institut fur Pharmakologie der BAYER AG, Wuppertal-Elberfeld, Germany **Psychotropic drugs as negative reinforcers.** Pharmacological Reviews. 27(3):419-428, 1975.

Experiments conducted to determine whether infusions of the psychotropic drugs LSD (lysergic acid diethylamide), STP (l-(2,5-dimethoxy-4-methyl-phenyl)2-propylamine-hydrochloride), chlorpromazine or impramine would function as negative reinforcers in the rhesus monkey are reported. The effects of these drugs in maintaining responding behavior that terminated either their infusion or stimuli associated with such infusion were compared with the effects of these drugs on responding maintained by comparable schedules of termination of electric shock. The findings indicate that infusions of psychotropic drugs can act as reinforcers independently of their effect on behavior engendered and maintained by other reinforcers. 15 references.

240021 McKearney, James W. Worcester Foundation for Experimental Biology, Shrewsbury, MA **Drug effects and the environmental control of behavior.** Pharmacological Reviews. 27(3):429-436, 1975.

Literature related to the experimental analysis of behavior controlled by drug administration is reviewed in the context of considerations generally important in the control of behavior by environmental events. It is noted that it is necessary to determine not which drugs serve as reinforcers but what factors determine whether or not any drug will serve as a reinforcer. Factors instrumental in establishing reinforcing or punishing conditions are analyzed. 24 references.

240022 Holz, W. C.; Gill, C. A. Smith, Kline and French Laboratories, Philadelphia, PA **Drug injections as negative reinforcers.** Pharmacological Reviews. 27(3):437-446, 1975.

Experiments on drugs as negative reinforcers are reviewed within the framework of operant conditioning principles. Prominent among these experiments are those involving responses maintained by termination of a drug infusion or a stimulus associated with such infusions. It is noted that the problems found in an analysis of drugs as negative reinforcers do not differ fundamentally from those found in other areas of operant analysis. Extraneous characteristics of stimuli influence their ability to control behavior and must be taken into consideration. The basic processes of response conditioning and elimination are shown to hold to the same form found in comparable procedures with electric shock. Control of responding by fixed-ratio schedules of terminating the stimulus associated with infusions have been demonstrated. The dose response relationships seem functionally equivalent to the stimulus intensity response relationships found with other noxious stimuli. 28 references.

240062 Davis, Michael; Sheard, Michael H. Yale University School of Medicine, 24 Park Street, New Haven, CT 06508 **p-Chloroamphetamine (PCA): acute and chronic effects on habituation and sensitization of the acoustic startle response in rats.** European Journal of Pharmacology (Amsterdam). 35(2):261-273, 1976.

In a series of six experiments, the effects of p-chloroamphetamine (PCA) on the acoustic startle response in rats were investigated. Fifteen minutes after 5mg/kg PCA, startle amplitude was inhibited; 2 to 15 hours after PCA, startle was facilitated. Rate of habituation was not altered. Both the inhibitory and excitatory effects of PCA were blocked by pretreatment with p-chlorophenylalanine but not with alpha-methylparatyrosine. Twenty four hours, one week and four weeks after PCA, initial startle amplitude was unchanged, but PCA increased rate or sensitization over successive tone blocks. Increased sensitization was most pronounced at 10mg/kg and absent at 2.5mg/kg. The early inhibitory effect of PCA, but not the later facilitatory effect, was eliminated by reducing the level of background noise. Results suggest that inhibition of startle sensitization is associated with enhanced release of serotonin, whereas enhancement of startle sensitization is associated with serotonin depletion. 41 references. (Author abstract modified)

240237 Szczawinska, Krystyna; Chodera, Alfons; Wojciak, Zofia; Kozaryn, Irena. Zaklad Farmakologii i Farmakodynamiki AM, 61-701 Poznan, Fredry 10, Poland **Changes in the pharmacodynamics and pharmacokinetics of psycholeptic drugs in radiation-sickness. Effect of X-ray radiation on pharmacodynamic activity of nitrazepam in animals.** Acta Physiologica Polonica (Warszawa). 26(5):523-527, 1975.

The anticonvulsive effect of nitrazepam was determined in animals exposed to a single 600 R radiation, and the exploring activity of the animals was studied after nitrazepam was administered during radiation sickness caused by this exposure.

On the first day after exposure the activity reducing effect was slightly weaker, but on the third and sixth days this effect was significantly stronger. The anticonvulsant effect of nitrazepam on the third day after exposure was significantly greater as compared with control animals, but on the sixth day no differences in the power of anticonvulsant activity between the two groups of animals was found. 13 references. (Author abstract)

240241 Post, Robert M. 3-West Clinical Research Unit, Section of Psychobiology, Adult Psychiatry Branch, NIMH, Rockville, MD 20852 **Clinical aspects of cocaine: assessment of acute and chronic effects in animals and man. (Unpublished paper).** Rockville, MD, NIMH, 1976. 33 p.

Different clinical effects of cocaine are discussed as they relate to both the dose and the duration of cocaine administration. The evolution of the cocaine effects with chronic administration and the evidence that many parameters demonstrate sensitization or reverse tolerance following repeated doses are emphasized. Studies of chronic cocaine in animals are reviewed in an attempt to elucidate mechanisms involved in the progressive effects and as they might be relevant models for the development of psychotic behavior. 66 references.

240750 Glick, S. D.; Zimmerberg, B.; Greenstein, S. Dept. of Pharmacology, Mount Sinai School of Medicine, CUNY, New York, NY 10029 **Individual differences among mice in normal and amphetamine-enhanced locomotor activity: relationship to behavioral indices of striatal asymmetry.** Brain Research (Amsterdam). 105(2):362-364, 1976.

An attempt was made to determine whether there is a relationship between locomotor activity and behavioral indices of striatal asymmetry in mice. One group of 24 mice was tested for side preferences and locomotor activity; a second group of 16 mice was tested for amphetamine induced rotation and locomotor activity. Results indicate significant inverse correlations between strength of side preferences and locomotor activity and between net rotations and locomotor activity. More active mice, both normally and after amphetamine, had lower indices of behavioral laterality than less active mice. To the extent that side preferences and rotation are manifestations of striatal asymmetry, these results suggest that individual differences in locomotor activity may be attributable to different degrees of such asymmetry. Degree of striatal asymmetry may be a primary determinant of individual differences in baseline activity and in sensitivity to the activity stimulant effect of amphetamine. 8 references.

240916 Houser, Vincent P.; Rothfeld, Benjamin; Varady, Alexander, Jr. RD 1, Box B95, Route 94, Chester, NY 10918 **Effects of chlorpromazine on fear-motivated behavior, urinary cortisol, urinary volume, and heart rate in the dog.** Psychological Reports. 38(1):299-308, 1976.

Development of a behavioral paradigm sensitive to the anxiolytic properties of drugs was attempted. Several doses of chlorpromazine were administered to dogs while they were subjected to a Sidman nondiscriminated avoidance schedule which contained seven conditioned stimuli/unavoidable shock (CS-US) pairings. The drug consistently reduced baseline response rate and enhanced shock rate. Facilitation of heart, response, and activity rates normally noted during the aversive CS were unaffected by administration of the drug. The overall heartrate, urinary volume, and urinary cortisol measures also showed no consistent pattern of results in response to drug administration. These results suggest that under this schedule of reinforcement only baseline response rate was sensitive to the anxiolytic effects of chlorpromazine. 20 references. (Author abstract modified)

241109 Sjursen, Frank H., Jr. University of Washington **Effects of cholinergic drugs on abnormal social behavior in the rhesus monkey. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-28445 HC$18.00 MF$7.50 245 p.

The effects of cholinergic drugs on abnormal social behavior in the rhesus monkey were examined to determine if a cholinergic inhibitory process underlies aberrant social behavior in isolate reared Ss. It was hypothesized that high levels of negative behavior, nonsocial behavior, passive behavior and rear responses of isolates would decrease when the anticholinesterase physostigmine was given, and that high levels of species typical positive behavior of peers would be decreased when atropine was given. Findings indicate that: 1) the cholinergic inhibitory system plays little role in modulating positive social behavior or negative social behavior in isolates or peer reared Ss; 2) they partially modulate social passive behavior in peer reared Ss, but not in isolates; 3) physostigmine increases nonsocial fear responses in isolates, suggesting that other cholinergic systems may underlie nonsocial fear responses; and 4) no drug effects occurred on activity level. A number of other findings are reported regarding the mechanism of action of the drugs, and possible relationships between specific atypical behaviors of autistic children and isolate reared monkeys are discussed. Failure to obtain the expected results is seen as possibly resulting from other neurochemical systems being involved, inadequate drug dosages, or insensitive behavioral measures. (Journal abstract modified)

241205 Smith, J. E.; Hingtgen, J. N.; Lane, J. D.; Aprison, M. H. Section of Basic Neural Sciences, Institute of Psychiatric Research, Indianapolis, IN 46202 **Neurochemical correlates of behaviour -- content of tryptophan, 5-hydroxytryptophan, serotonin, 5-hydroxyindoleacetic acid, tyrosine, dopamine and norepinephrine in four brain parts of the pigeon during behavioural depression following an injection.** Journal of Neurochemistry (Oxford). 26(3):537-541, 1976.

In a study of the neurochemical correlates of behavior, pigeons working on a multiple fixed-ratio 50, fixed-interval 10 schedules of food reinforcement were injected with L-tryptophan and killed at various times before, during and after the period of behavioral depression following the administration of this amino acid. The levels of tryptophan, 5-hydroxytryptophan, 5-hydroxytryptamine, 5-hydroxindoleacetic acid, tyrosine, dopamine and norepinephrine were concurrently measured in four specific areas of the brain (telencephalon, diencephalon plus mesencephalon, pons plus medulla oblongata and cerebellum). The course of the increases in the level of 5-hydroxytryptamine in the telencephalon, and subsequent return to preinjection levels, was temporally related to the onset of the decreased responding and gradual return to normal rates of responding. Changes in dopamine and norepinephrine were not correlated with the onset of and recovery from the decreased response rates. The data are discussed in terms of previously reported work with 5-hydroxytryptophan and the importance of the telencephalic serotonergic system in certain types of behavioral depression. 32 references. (Author abstract)

241221 Tetsche, Kaj; Fjerdingstad, E. J.; Fjerdingstad, Erik. Dept. of Anatomy B, Univ. of Aarhus, DK-8000 Aarhus, C, Denmark **Euflavine: effect on brain heavy metal content and**

staining pattern, and on shuttle box behavior in goldfish. Psychopharmacologia (Berlin). 46(2):123-126, 1976.

The effect of euflavine on brain heavy metal content and staining pattern, and on shuttlebox behavior in goldfish was examined. Goldfish were exposed to euflavine for one hour to 14 days. The treatment resulted in a reduced stainability of the brain with the Timm histochemical procedure for heavy metals. In contrast, analysis of flameless atomic absorption spectrophotometry showed no significant changes in the concentrations of zinc and copper after eufluvine treatment. In the shuttlebox, a significant increase in general activity was found. The results indicate that such drugs do not cause a true depletion of heavy metals in the brain. 18 references. (Author abstract)

241223 Laschka, E.; Herz, A.; Blasig, J. Department of Neuropharmacology, Max-Planck-Institut fur Psychiatrie, D-8000 Munich 40, Kraepelinstrasse 2, Germany **Sites of action of morphine involved in the development of physical dependence in rats: I. Comparison of precipitated morphine withdrawal after intraperitoneal and intraventricular injection of morphine antagonists.** Psychopharmacologia (Berlin). 46(2):133-139, 1976.

In rats made dependent on morphine by implantation of morphine pellets, withdrawal, as precipitated by intraventricular injection of morphine antagonists, was compared to withdrawal as precipitated by systemic antagonist application. The results, most clearly those obtained with a hydrophilic compound, diallyl-normorphinium-bromide, point to periventricularly located sites of action for the release of most withdrawal signs by antagonists. Jumping, reaching only low levels after injection of levallorphan and nalorphine, was very pronounced when the benzomorphane derivative SH-254, was used. In the case of writhing and diarrhea, the situation is more complicated. Possibly, central as well as peripheral mechanisms are involved in the expression of these signs. 27 references. (Author abstract)

241224 Papeschi, R.; Theiss, P.; Ayhan, H. Ospedale Psichiatrico Provinciale, I-55050 Maggiano (Lucca), Italy **AMT catalepsy and hypokinesia: interaction with morphine and cocaine.** Psychopharmacologia (Berlin). 46(2):149-157, 1976.

The interaction of morphine and cocaine with alpha-methyl-p-tyrosine (AMT) catalepsy was examined in rats. Acute morphine induced a dose dependent hypokinesia and rigidity, but only midl and non dose dependent catalepsy. AMT, injected after morphine, slightly potentiated catalepsy but not hypokinesia during 3 hr after morphine; in contrast, rigidity was decreased. The behavioral changes induced by AMT were accelerated in onset and reached their usual development, although AMT toxicity and hypothermia were completely antagonized. It is therefore suggested that AMT hypokinesia/catalepsy are not the consequence of toxicity. When morphine was injected 4 hr after AMT, a mutual potentiation of the two drugs on hypokinesia and catalepsy was observed. Rigidity appeared to be antagonized. After 17 days of repeated injections, morphine no longer elicited hypokinesia and catalespy, but no cross-tolerance developed to the AMT behavioral changes. A similar lack of cross-tolerance to the effects of AMT or haloperidol was observed when morphine tolerance was induced by pellet implantation. Catalepsy and hypokinesia developed in a much more pronounced way after two large i.p. doses than after small multiple administration of AMT. The hyperthermic response observed after a 40mg/kg s. c. injection of morphine was reversed to hypothermia when the same dose was given 4 to 10 hr after catecholamine synthesis inhibition. Cocaine strongly antagonized AMT hypokinesia and catalepsy when given after AMT. 32 refrences. (Author abstract modified)

241225 Sanders, Barbara; Collins, Allan C.; Wesley, Victor H. Institute for Behavioral Genetics, University of Colorado, Boulder, CO 80302 **Reduction of alcohol selection by pargyline in mice.** Psychopharmacologia (Berlin). 46(2):159-162, 1976.

The effects of p-chlorophenylalanine (PCPA) on alcohol selection were compared with those of pargyline, a monoamine oxidase inhibitor which increases brain levels of 5-hydroxytryptamine(5-HT). Ingestion of a 10% ethanol solution was assessed in male C57BL/6J mice given daily injections of 250 or 300mg/kg PCPA, 50mg/kg pargyline, or saline. An additional control group received no treatment. A two bottle preference procedure was employed, and ethanol and water intake were recorded during a pretreatment period (11 days), a treatment period (8 days, and a posttreatment period (10 days). Like other agents which increase 5-HT, pargyline produced a depression in ethanol intake which lasted beyond the time of drug administration. PCPA had no effect on ethanol ingestion either during the period of drug administration or afterwards. 11 references. (Author abstract modified)

241227 Senault, B. Department de Pharmacologie, Laboratoire Le Brun, 41 bis, Bd. Anatole-France, F-93300 Aubervilliers, France **/Amantadine: aggressive effect; effect on apomorphine-induced aggressivity in the rat./** Amantadine: effet agressogene propre; effet sur l'aggressivite induite par l'apomorphine chez le rat. Psychopharmacologia (Berlin). 46(2):167-168, 1976.

The effects of amantadine on aggressive behavior induced by apomorphine were examined in rats. Only amantadine in doses of 10mg/kg i.v. and 50mg/kg i.p. induced a very slight aggressive effect, but in doses of 30 and 50mg/kg i.p. it inhibited the aggressive behavior induced by 1mg/kg apomorphine. The effect was dose related and it was more pronounced when amantadine (50mg/kg i.p.)was injected 30 min rather than 1 hr before apomorphine. 8 references. (Author abstract modified)

241228 Colpaert, Francis C.; Niemegeers, Carlos J. E.; Janssen, Paul A. J. Department of Pharmacology, Janssen Pharmaceutica, Research Laboratories B-2340 Beerse, Belgium **Theoretical and methodological considerations on drug discrimination learning.** Psychopharmacologia (Berlin). 46(2):169-177, 1976.

A method is described which allows the assessment of discriminative stimulus properties of drugs, and the ability of amphetamine chlordiazepoxide, desipramine and haloperidol to produce a discriminative stimulus complex (DSC) is evidenced. The method yielded clear cut data that are specifically related to drug discrimination learning without being possibly confounded by state dependent effects. In addition, the experimental procedure is designed to provide an appropriate measurement of operant response modulating drug effects. 23 references. (Author abstract)

241229 Wauquier, Albert; Niemegeers, Carolos J. E. Department of Pharmacology, Janssen Pharmaceutica, Research Laboratories, B-2340 Beerse, Belgium **Intracranial self-stimulation in rats as a function of various stimulus parameters: VI. Influence of fentanyl, piritramide, and morphine on medical forebrain bundle stimulation with monopolar electrodes.** Psychopharmacologia (Berlin). 46(2):179-183, 1976.

The effects of different subcutaneous doses of fentanyl, pitramide, and morphine on self-stimulation in rats were studied. Different stimulus parameter combinations (SPC) inducing low, high, or intermediate control response rates (CRR) were applied during the same experimental sessions. The three narcotic analgesics induced response depression (RD) and response stimulation (RS). RS was mostly observed at low dose levels; RD was dose related. SPC's inducing low CRR were more sensitive than those inducing high CRR. Fentanyl was more potent than piritramide and than morphine. The RD is related to motor incapacitation, as the doses needed to effectively reduce self-stimulation also induced obvious catatonia. It is suggested that the RS is a more specific effect reflecting sensitization of structures involved in reinforcement of behavior. 25 references. (Author abstract)

241231 Jahn, Ulrich; Mixich, Georg. Laboratorien fur Arzneimittelforschung der Siegfried AG, CH-4800 Zofingen, Switzerland /**Wet dog shake behavior in normal rats, elicited by benzylideneaminooxycarbonic acid derivatives.**/ Benzylidenaminooxy-Carbonsaure-Derivate als Ausloser von "Wet Dog Shake"-Verhalten bei normalen Ratten. Psychopharmacologia (Berlin). 46(2):191-196, 1976.

The capability to produce wet dog shaking behavior (WDS), known as the morphine withdrawal syndrome, was correlated with a specific chemical structure among benzylideneaminooxycarbonic acid derivatives. The threshold dose of the most effective agents was 25-50mg/kg, rather independent of the mode of application. Maximal responses of 10-20 WDS per min and per animal were reached after application of 100-200mg/kg. WDS behavior appeared within the first minutes after dose and lasted up to several hours. Detailed information is given on WDS action of the substance Sgd-8473 (alpha-((4-chlorobenzylideneamino)-oxy)-isobutyric acid) and the influence by different pharmacologic agents thereon. Inhibition of WDS was produced by: narcotic analgesics, narcotic antagonists, psychosedative drugs, yohimbine, dl-amphetamine, cocaine, apomorphine and clonidine. Without influence on WDS were: physostigmine, atropine, ganglionic or adrenergic blocking drugs, dopa, monoamine oxidase inhibitors, serotonin and histamine antagonists, and nonnarcotic analgesics. To some extent chemically induced WDS seemed to be susceptible like precipitated WDS. Sgd-8473 could be qualified for differentiating narcotic and nonnarcotic analgesics, for a quasi-abstinence agent in research on dependence mechanisms and for a tool in neuroanatomical studies of the central nervous system. 14 references. (Author abstract)

241241 Sanghvi, I.; Geyer, H.; Gershon, S. Neuropsychopharmacology Research Unit, Dept. of Psychiatry, New York Univ. Medical Center, 550 First Ave., New York, NY 10016 **Exploration of the antidepressant potential of iprindole.** Life Sciences (Oxford). 18(6):569-574, 1976.

Iprindole, a tricyclic indole compound with an antidepressant activity, was evaluated in an animal test model. It was predicted that iprindole would potentiate the behavioral and cardiovascular effects of yohimbine, a naturally occurring indole alkaloid, in conscious dogs. For comparison, imipramine, a standard antidepressant drug was used. Iprindole was tested at a dose of 3, 9, and 15mg/kg, and it potentiated the behavioral and cardiovascular effects of yohimbine at a dose of 9mg/kg. Iprindole failed to potentiate norepinephrine response in dogs; it is noted that similar observations have been reported in man. The results further confirm the validity of the present test for evaluation of potential antidepressant agents in the conscious dog. 24 references. (Author abstract)

241243 Carder, Brooks; Cheng, Rosalie Shall-Way. Synanon Foundation, Inc., Marshall, CA 94940 **Behavioral disinhibition by mescaline.** Life Sciences (Oxford). 18(6):585-591, 1976.

To demonstrate behavioral disinhibition by mescaline, rats were exposed to a conditioned emotional response (CER) procedure in which sucrose drinking was suppressed by a tone previously paired with shock. Suppression of drinking during the tone was reduced by mescaline (50mg/kg) independently of whether training took place under mescaline or placebo. Additional drinking indicate that the result could not be distributed to an increased drive to drink sucrose. It is proposed that mescaline releases behavior from inhibitory control. A number of studies from the literature are cited which support this hypothesis. 12 references. (Author abstract)

241244 Goldstein, Avram; Pryor, Gordon T.; Otis, Leon S.; Larsen, Ferol. Addiction Research Foundation, Palo Alto, CA **On the role of endogenous opioid peptides: failure of naloxone to influence shock escape threshold in the rat.** Life Sciences (Oxford). 18(6):599-604, 1976.

In a study of the role of endogenous opioid peptides, rats were trained to avoid footshock and were then administered naloxone in varying doses to determine its impairment of avoidance performance. It was hypothesized that blocking of opiate receptors by naloxone would lower the shock escape threshold, but rats treated with doses of naloxone sufficient to block morphine analgesia showed no change in the threshold for escape from footshock. The data offer no support to the hypothesis that an endogenous opioid modulates responsiveness to pain and discomfort. 18 references. (Author abstract modified)

241245 Hitzemann, Barbara A.; Hitzemann, Robert J.; Brase, David A.; Loh, Horace H. Dept. of Pharamcology, University of California, San Francisco, CA 94143 **Influence of prenatal d-amphetamine administration on development and behavior of rats.** Life Sciences (Oxford). 18(6):605-612, 1976.

The influence of prenatal d-amphetamine administration on the development and behavior of rats was investigated. Beginning on the fifth day of gestation, rats were administered d-amphetamine sulfate twice daily until term. The administration of d-amphetamine caused a dose related increase in pup mortality, however the increase in pup death could not be correlated with any gross pathological signs. Surviving pups were analyzed for changes in motor behavior and brain biogenic amine levels. It was found that the amphetamine offspring showed a marked reduction in the ability to habituate to new surroundings, and this effect persisted for at least 3 months after birth. On day 35, brain levels of norepinephrine in the amphetamine offspring were decreased 21%. On day 84, in the amphetamine offspring norepinephrine levels were reduced 18% in both the diencephalon and brainstem; dopamine levels were reduced 21% in the brainstem compared to control offspring. 14 references. (Author abstract)

241250 Downs, David A.; Woods, James H. Dept. of Pharmacology, University of Michigan Medical School, Ann Arbor, MI 48104 **Morphine, pentazocine and naloxone effects on responding under a multiple schedule of reinforcement in rhesus monkeys and pigeons.** Journal of Pharmacology and Experimental Therapeutics. 196(2):298-306, 1976.

The effects of morphine, pentazocine, naloxone and combinations of these drugs on schedule controlled behavior were examined in rhesus monkeys (Macaca mulatta) and pigeons. The order of potency in decreasing response rates under a

multiple 5 minute fixed-interval, 30 response fixed-ratio schedule in both monkeys and pigeons was morphine greater than pentazocine greater than naloxone. Compared to monkeys, pigeons were less sensitive to morphine and pentazocine and slightly more sensitive to naloxone. In monkeys and pigeons, as the morphine dose increased, higher naloxone doses were required to restore responding to or near control levels. In pigeons, however, the response rate decreases caused by naloxone prevented the complete antagonism of the highest morphine dose and limited the range of naloxone doses over which complete antagonism of morphine occurred. Antagonism of pentazocine by naloxone generally was greatest at the lowest pentazocine dose tested in both monkeys and pigeons. 17 references. (Author abstract modified)

241251 Yunger, Libby M.; Harvey, John A. CNS Disease Therapy Section, 56B-137, Lederle Laboratories, Pearl River, NY 10965 **Behavioral effects of L-5-hydroxytryptophan after destruction of ascending serotonergic pathways in the rat: the role of catecholaminergic neurons.** Journal of Pharmacology and Experimental Therapeutics. 196(2):307-315, 1976.

The behavioral effects of L-5-hydroxytryptophan after destruction of ascending serotonergic pathways in the rat were examined. Lesions in the medial forebrain bundle of the rat produced a 68% to 74% decrease in telencephalic serotonin (5-HT) and a 30% to 43% decrease in jump threshold. L-5-Hydroxytryptophan (L-5-HTP) returned the 5-HT content and jump threshold of lesioned rats to normal levels. Pretreatment with 6-hydroxydopamine (6-OHDA) which selectively destroys catecholamine neurons, had no effect on the jump threshold of nonlesioned rats, nor did it further change the 5-HT content or jump threshold of lesioned rats. Lesioned rats pretreated with 6-OHDA demonstrated an increase in 5-HT content after L-5-HTP. Thus, 6-OHDA pretreatment significantly decreased the net accumulation of 5-HT from L-5-HTP in nonlesioned rats. These rats also demonstrated further decreases in norepinephrine and dopamine content after L-5-HTP. It is concluded that L-5-HTP can be decarboxylated to 5-HT in serotonergic and catecholaminergic neurons and that the behavioral effects of L-5-HTP in lesioned rats may be due to the formation of 5-HT in catecholaminergic neurons where it may act as a false transmitter. 49 references. (Author abstract modified)

241258 Johansson, J. O.; Jarbe, T. U. C. Department of Pharmacology, University of Uppsala, Uppsala, Sweden **Physostigmine as a discriminative cue in rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 219(1):97-102, 1976.

The use of physostigmine as a discriminative cue in rats is reported. Rats trained to respond differentially in a T-maze contingent upon the presence or absence of physostigmine showed a reversal of drug responding when physostigmine was given simultaneously with the anticholinergic ditran. Testing the quaternary anticholinesterase neostigmine resulted in no drug responding, which indicates a central site of action for the physostigmine discrimination. 12 references. (Author abstract)

241300 Phillips, Anthony G.; Fibiger, Hans C. Dept. of Psychology, University of British Columbia, Vancouver, British Columbia, V6T 1W5, Canada **Long-term deficits in stimulation-induced behaviors and self-stimulation after 6-hydroxydopamine administration in rats.** Behavioral Biology. 16(2):127-143, 1976.

Rats with electrodes implanted in the lateral hypothalamus were screened for stimulation induced feeding, drinking, and/or gnawing. Animals displaying one or more of these behaviors were given additional tests for self-stimulation. Following a series of preoperative tests, animals were assigned to experimental or control groups, with the former receiving an intraventricular injection of 6-hydroxydopamine (6-OHDA) plus pretreatment with the monoamine oxidase inhibitor tranylcypromine, while the control animals were treated with tranylcypromine prior to vehicle injections into the ventricles. 6-OHDA injections reduced whole brain dopamine and noradrenaline to 19% and 24% of control values, respectively. This reduction of brain catecholamines was accompanied by a transient adipsia and hypophagia and a long-term disruption of stimulation induced feeding, drinking, and gnawing. The similarity between brain stimulation induced behavior, tail pinch-induced behavior, and amphetamine stereotypy are discussed, along with their possible dependence on a common neurochemical substrate. 34 references. (Author abstract modified)

241301 Hall, Michael E. Dept. of Physiology and Biophysics, School of Medicine, University of Miami, Miami, FL 33124 **The effects of norepinephrine biosynthesis inhibition on the consolidation of two discriminated escape responses.** Behavioral Biology. 16(2):145-153, 1976.

In a study of the effects of norepinephrine biosynthesis on behavior, male and female mice were treated with diethyldithiocarbamate, a dopamine-beta-hydroxylase inhibitor, immediately following training on two discriminated shock escape tasks. Mice trained on a position discrimination task to criteria of either 3 out of 4 or 9 out of 10 consecutive errorless escapes were unaffected by treatment with diethyldithiocarbamate. Mice trained on a light/dark discrimination task to a criterion of 5 out of 6 consecutive errorless escapes and treated with diethyldithiocarbamate were significantly poorer in terms of savings scores than control mice when tested a week later. Mice similarly trained on the light/dark discrimination to a criterion of 9 out of 10 consecutive errorless escapes and treated with diethyldithiocarbamate did not differ significantly from control mice. When treatment with diethyldithiocarbamate was delayed for an hour after training to a criterion of 5 out of 6 consecutive errorless escapes, such treatment was ineffective. 39 references. (Author abstract)

241307 Liebman, Jeffrey M.; Segal, David S. Psychiatry Dept., School of Medicine, University of California, San Diego, La Jolla, CA 92093 **Lack of tolerance or sensitization to the effects of chronic d-amphetamine on substantia nigra self-stimulation.** Behavioral Biology. 16(2):211-220, 1976.

The effects of repeated administration of d-amphetamine on intracranial self-stimulation were investigated through substantia nigra electrodes in rats. Doses of d-amphetamine which facilitated bar-pressing for self-stimulation on the first day of treatment were administered 30 minutes before daily testing for 10 to 12 days. Self-stimulation rates on the last day of treatment did not differ significantly from those on the first day at any dose tested. These results are in contrast to previous reports of progressive facilitation of locomotor activity and stereotypy by repeated d-amphetamine administration. To the extent that self-stimulation in substantia nigra reflects the functional state of dopaminergic neurotransmission, progressive augmentation of activity and stereotypy by repeated d-amphetamine administration may not involve dopaminergic processes. 23 references. (Author abstract)

241311 Jerussi, Thomas P.; Glick, Stanley D. Dept. of Pharmacology, Mount Sinai School of Medicine, CUNY, 5th Ave. and 100th St., New York, NY 10029 **Spontaneous and drug-induced rotation (circling behavior) in the Mongolian gerbil (Meriones unguiculatus).** Behavioral Biology. 16(2):241-244, 1976.

Eight normal gerbils were tested for spontaneous and drug induced rotation in an automated rotometer. When tested without any drug every other day for five test sessions, each gerbil displayed significant rotation that was consistent in direction and magnitude from session to session. Apomorphine and d-amphetamine potentiated, whereas haloperidol antagonized the animals' spontaneous rotational behavior. The occurrence of spontaneous rotation in gerbils suggests that gerbils have normally a much larger asymmetry in nigrostriatal function. 17 references. (Author abstract modified)

241314 Sung, Y. F.; Holtzman, S. G. Department of Anesthesiology, Emory University, Atlanta, GA 30322 **Effects of intravenous anesthetics on continuous avoidance behavior in the rat.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 219(2):243-250, 1976.

The actions of ketamine, etoxadrol and thiopental on continuous avoidance behavior in the rat were evaluated following i.v. administration. Ketamine and thiopental exerted only a depressant effect on avoidance behavior which was attributable to the anesthetic properties of the drugs. Biphasic activity was displayed with etoxadrol; avoidance responding was increased at low doses and decreased at high doses. A persistent rebound stimulation of responding occurred upon recovery from the anesthetic effect of high doses of etoxadrol. The effects of these drugs on continuous avoidance behavior do not correlate with reported effects on the disposition of brain monoamines. 15 references. (Author abstract)

241330 Zinkin, Sheila; Lecanuet, Jean-Pierre; Deweer, Bernard. Laboratoire de Physiologie nerveuse, Centre National de la Recherche Scientifigue, 91190 Gif-sur-Yvette, France **Retroactive and proactive effects of anaesthesia on following in chicks.** Physiology & Behavior. 16(2):185-189, 1976.

The retroactive and proactive effects of halothane anesthesia on imprinting were examined in chicks. Results reveal that halothane, administered after imprinting sessions in day old chicks, produces two different effects on following response behavior tested 3 days later. First, it delays the onset of the following response for animals treated immediately after imprinting. Second, it disturbs the general performance of the following response, an effect apparently unrelated to the time of treatment. It is suggested that only the first of these effects reflects a disturbance of retention. 5 references. (Author abstract modified)

241349 Shah, Nandkumar S. Ensor Foundation Research Laboratory, William S. Hall Psychiatric Institute, Columbia, SC 29202 **Influence of psychotropic drugs and beta-diethylaminoethyl-diphenylpropylacetate (SKF 525-A) on mescaline-induced behavior and on tissue levels of mescaline in mice.** Biochemical Pharmacology (Oxford). 25(2):591-597, 1976.

The effects of psychotropic drugs of beta-diethylaminoethyl-diphenylpropylacetate (SKF-525-A) on mescaline induced behavior and on the brain, plasma, liver and eye levels of mescaline were studied in mice. Lower doses of promazine, trifluoperazine, and diazepam were not effective antagonists of mescaline induced increased locomotor activity or scratching responses. Mesoridazine and diazepam partially prevented mescaline induced gross behavior, effectively blocked scratching responses to mescaline, produced no cataplepsy and did not elevate tissue mescaline contents. Higher doses of trifluoperazine, mesordiazine, and promazine blocked not only the activity increasing effects of mescaline but also the normal locomotor movements; with the exception of 30mg/kg of mesoridazine, these treatment schedules induced a cataleptic like state and markedly enhanced tissue levels of mescaline, SKF-525-A potentiated the mescaline antagonizing effects and mescaline retaining activity of several compounds listed. 38 references. (Author abstract modified)

241363 Ueki, Showa; Fujiwara, Michihiro; Yamamoto, Tsuneyuki. Dept. of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka 812, Japan **Symposium II. Pharmacology on brain monoamines: 4) the role of brain serotonin in emotional behavior of the rat.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):13P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, changes in emotional behavior following lesions of the midbrain raphe nuclei were reported in rats. Lesions were created in either the dorsal raphe (DR) or median raphe (MR), and in both dorsal and median raphe nuclei (DR-MR). Locomotor activity was not changed by DR lesion, but was significantly increased by MR lesion, and extremely increased by DR-MR lesions. Hyperactivity of MR lesioned rats was further increased by p-chlorophenylalanine (PCPA), methamphetamine and atropine, and was decreased by alpha-methyl-p-tyrosine, chlorpromazine and haloperidol, but was not changed by L-dopa. Raphe lesioned rats showed the hyperemotional responses to various stimuli. Muricide was induced after raphe lesions, with the incidence being greatest in DR-MR lesioned rats. Tetrahydrocannabinol also induced muricide in rats after intraventricular administration of 5,6-dihydroxytryptamine. Results suggest that brain serotonin plays an inhibitory role in locomotor activity as well as in aggressive behavior, and its decrease is closely related to the occurrence of muricide, particularly of mouse eating behavior. (Author abstract modified)

241364 Miyauchi, Tatsuo; Ozawa, Hikaru. Department of Chemical Pharmacology, Pharmaceutical Institute, Tohoku University, Sendai 980, Japan **The potentiating effect of LiCl on adrenergic drug-induced aggressive behavior in mice.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):19P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the mechanisms of action of lithium chloride (Licl) on aggressive behavior in rats were reported. Nialamide + L-dopa produced an increase in contents of brain norepinephrine (NE), dopamine (DA) and serotonin (5-HT). Aggression induced by this treatment was completely blocked by phenoxybenzamine (PBZ) and by disulfiram (DSR) which inhibited the increase in NE. p-Chlorophenylalanine (p-CPA), which abolished the increase in 5-HT, increased the aggression. Clonidine induced an aggression without affecting the contents of three brain monoamines, and this aggression was inhibited by PBZ and increased by DSR which decreased the content of NE. LiCl potentiated the aggression induced by both nialamide + L-dopa and clonidine. Although LiCl did not alter the levels of three brain monoamines, it increased the turnover of NE and decreased the content of endogenous normetanephrine. It is concluded that lithium reduces the ability of nerve ending vesicles to store NE, leading to increased metabolism and turnover and decreased concentration of NE at receptor sites. (Author abstract modified)

241367 Hara, Chiaki; Watanabe, Shigenori; Ueki, Showa. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Kukuoka 812, Japan **Effects of drugs injected into the hypothalamus on muricide and EEG in the olfactory bulbectomized rats.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):45P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, effects of drugs injected into the hypothalamus on muricide and electroencephalography (EEG) in the olfactory bulbectomized rats were reported. Bipolar electrodes in the frontal cortex and cannulae for drug injection were permanently implanted in the lateral preoptic area (POA), the posterior portion of the lateral hypothalamus (p-LH) and mammillary body (MB). The effects of drugs injected into the hypothalamus on muricide and neocortical EEG activity were simultaneously examined. Chlorpromazine (CPZ) injected into either POA or p-LH suppressed muricide and induced the EEG drowsy pattern which was similar to that observed upon i.p. injection. Chlordiazepoxide (CDP) inhibited muricide only when injected into MB, and also evoked the EEG drowsy pattern. Atropine (AT), imipramine (IMP) and amitriptyline (AMT) significantly inhibited muricide without causing the EEG drowsy pattern when applied in p-LH. These effects of IMP and AMT were similar to those obtained with i.p. injection, but AT elicited the EEG drowsy pattern when administered i.p. Results suggest that the hypothalamus is an important site of antimuricidal action of these drugs, and this action of CPZ and CDP is related to an inhibition of the arousal system in the brain, while IMP and AMT act differently from CPZ and CDP regarding neural mechanisms. (Author abstract modified)

241370 Suzuki, Masahiko; Nabeshima, Toshitaka; Kameyama, Tsutomu. Dept. of Chemical Pharmacology, Faculty of Pharmaceutical Sciences, Meijo University, Nagoya 468, Japan **Studies on biogenic amines and behavior (I). Relationship between brain monoamines and defecation in rats.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):47P-48P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the emotional defecation correlation to biogenic amines was reported in rats. 5-Hydroxytryptophan (5-HTP) significantly decreased defecation but locomotor activity was not affected with the drug. Rats pretreated with DL-p-chlorophenylalanine (p-CPA) tended to show an increase in the number of fecal boluses excreted. 5-Hydroxytryptamine (5-HT) was equally effective in diminishing the open-field (OF) performance of p-CPA treated rats. The inhibitory effects of 5-HTP on defecation were enhanced after depletion of biogenic amines by reserpine treatment. Since it is quite possible that catecholamines may be responsible for the emotional defecation, the effects of L-dopa, DL-alpha-methyl-p-tyrosine (MT) or methamphetamine on the defecation were investigated. L-Dopa and methamphetamine decreased the number of fecal boluses and fecal elimination after MT injection was normal. These results suggest that the defecation after emotional stimulation is due to a change in the biogenic amine level in the brain. (Author abstract modified)

241371 Nabeshima, Toshitaka; Suzuki, Masahiko; Kameyama, Tsutomu. Department of Chemical Pharmacology, Faculty of Pharmaceutical Sciences, Meijo University, Nagoya 468, Japan **Studies on biogenic amines and behavior (II). Relationship between emotionality and defecation.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):48P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of 5-hydroxytryptamine (5-HT) on nonemotional defecation were reported in rats. The number of fecal boluses deposited and food consumption in isolated and group housed rats in their home cages after DL-p-chlorophenylalanine (p-CPA) were recorded. Animals on a vehicle only showed a decrease in both scores during the day and an increase in these scores at night. Animals treated with p-CPA tended to show diminishing effects in this circadian rhythm. That is, the p-CPA treated animals defecated no more than did the controls in a familiar cage. When tested in the open-field (OF) after p-CPA injection, the treated rats defecated more than the controls throughout the 4 day experimental period. 5-HTP increased the number of fecal boluses elimination compared with the control, 0-30 min after the injection in home cage rats. However, fecal elimination 30-120 min after injection was normal. After intraventricular injection with 5-HT or 5-hydroxytryptophan (5-HTP), the fecal excretion was significantly reduced compared with the control. It is concluded that the defecation which occurred in OF is emotional defecation. Thus, the reduction in emotional defecation may be due to an increase in brain 5-HT. (Author abstract modified)

241372 Yamada, Katsushi; Suenaga, Noriko; Takishita, Shuichi; Fukuda, Takeo. Department of Pharmacology, Faculty of Medicine, Kyushu University, Fukuoka 812, Japan **Actions of 6-hydroxydopamine injected intraventricularly into developing rats (2). Influence on motor activities and aggressive behavior.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):48P-49P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, motor activities and emotional responses of adult rats treated with 6-hydroxydopamine (6-OHDA) in the suckling period were reported. Runwheel activity (count of rotation of the wheel) of 6-OHDA treated rats was significantly lower than that of control rats in both light time and dark time. After a low dose of methamphetamine, the activity increased significantly only in the treated rats. A large dose of methamphetamine produced a marked increase of the activity in both groups, but the activity of the treated rats was significantly higher than that of control rats. In the open-field test, ambulation and rearing within 3 min were not significantly altered by 6-OHDA treatment, whereas fast decline in ambulation was noted in the treated rats during the continuous observation of 30 min. In the experiment of emotional behavior, increased startle response to tail pinching or increased struggling and vocalization during capture were observed in 6-OHDA treated rats. (Author abstract modified)

241373 Nakahara, Hajime; Segawa, Mitsuru; Shiomi, Hirohito; Takagi, Hiroshi. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto 606, Japan **Effect of delta9-tetrahydrocannabinol on the metabolism of brain monoamines with special reference to the relationship between noradrenaline contents of the olfactory bulb and muricide behavior.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):49P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the correlation between changes in the levels of monoamines and their metabolites in several regions of the brain and occurrence of tetrahydrocannabinol (THC) induced muricide in rats was reported. THC was given i.p. to rats isolated and fasted for 24 hr. At a dose of 20mg/kg, THC showed the maximum muricide behavior 60 to 90 min after administration in 55% of rats with recovery within 3 hr. Animals were sacrificed 60 to 90 min after the THC injection and contents of

monoamines and their metabolites were fluorometrically determined. THC treated rats were divided into two groups: muricide (m(+)) and nonmuricide (m(-))rats. In the olfactory bulb of m(+) rats, noradrenaline content changed, but such changes were not observed in m(-) rats. 5-Hydroxytryptamine and 5-hydroxyindoleacetic acid contents in the olfactory bulb decreased in both m(+) rats and m(-) rats. Results suggest that decreased noradrenergic nervous activity is related to the manifestation of THC induced muricide behavior. (Author abstract modified)

241374 Hata, Taeko; Okage, Tazuko; Kita, Tomitaro; Handa, Takeshi; Yoneda, Ryozo. Department of Pharmacology, Faculty of Pharmacy, Kinki University, Higashi Osaka 577, Japan **Central nervous depressive actions of neurotropin on mice and rats.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):50P, 1975

At the 48th general meeting of the Japanese Pharmacological Society, the pharmacological actions of neurotropin (NSP), an extract isolated from vaccinia virus injured skin of rabbits were reported. In the small intestine isolated from mice, NSP slightly accelerated peristalsis, and to some extent increased acetylcholine (ACh) induced contraction, but had no influence on adrenaline induced relaxation. NSP slightly antagonized histamine induced contraction in the small intestine and in tracheal muscle from guinea-pig. Spontaneous motor activities in mice were decreased and exploratory movements were slightly decreased with NSP. Sleeping time induced by sodium methylhexabital in mice was prolonged by pretreatment of NSP. While NSP had no influence on normal blood pressure of Wistar rats, high blood pressure in spontaneously hypertensive rats was gradually reduced by NSP, dose dependently. The blood pressure did not fall below normal levels with NSP. NSP reduced tremorine induced tremor in mice and had no reducing influence on perphenazine induced catatonia in rats. Results suggest that NSP has central depressive effects. (Author abstract modified)

241375 Kamei, Chiaki; Fujitani, Yasuko; Oka, Makoto; Shimizu, Masanao. Department of Pharmacology, Research Laboratories, Dainippon Pharmaceutical Co., Ltd., Suita, Osaka 564, Japan **Comparison of the effects of neuroleptics on self-stimulation and conditioned avoidance response in rats.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):50P-51P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of certain neuroleptics on hypothalamic self-stimulation in rats were reported and compared with the effects on conditioned avoidance response. Chlorpromazine and perphenazine (phenothiazine derivatives) depressed the self-stimulation and avoidance response at the same dose levels. Haloperidol and trifluperidol (butyrophenone derivatives) depressed the self-stimulation at doses smaller than those which depressed the avoidance response. Clothiapine and clozapine (dibenzoheteropine derivatives) and oxypertine (indole derivatives) depressed the self-stimulation at doses larger than those which depressed the avoidance response. These results suggest that neuroleptics can be classified into three groups, based on a ratio of the effect on self-stimulation to conditioned avoidance response. (Author abstract modified)

241376 Kuribara, Hisashi; Okuizumi, Kiyoko; Shirota, Michiko; Tadokoro, Sakutaro. Behavior Research Institute, School of Medicine, Gunma University, Maebashi 371, Japan **Behavioral effects of penfluridol in rats.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):51P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of penfluridol, a diphenylbutylpiperidine type psychotropic agent, on operant behavior were reported and compared with those of chlorpromazine and haloperidol in rats trained on the following schedules. Fixed-ratio (FR 30) schedules food reinforcement and differential reinforcement of low rate of water reinforcement (DRL 20 sec) schedules were used for positively reinforced behavior. Continuous (Sidman type) and discriminated avoidance schedules were used for negatively reinforced behavior. Conditioned suppression of response (CER) under FR 30 developed by stimulus presentation with electric shock was also applied. When 1mg/kg of penfluridol was given orally, no change was observed in response of all the performances. At higher doses, the responses were inhibited dose dependently except for the DRL performance, in which only correct response rate decreased at 8mg/kg. These inhibitory effects were observed more readily in the negatively reinforced behavior than in those which were positive. These behavioral effects suggest that penfluridol has neuroleptic properties similar to those of chlorpromazine or haloperidol. In general, the inhibitory effects reached the maximum level at 16 hr and lasted for 2-3 days after oral administration of the drug. (Author abstract modified)

241377 Shimizu, Shin-ichiro; Kishi, Reiko. Department of Pharmacology, Hokkaido University School of Medicine, Sapporo 060, Japan **Differential sensitivity of the response duration and response rate to imipramine during operant behavior in rats.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):51P-52P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of imipramine on the response duration and response rate of lever pressing behavior in rats were reported. Male albino rats of Wistar strain were deprived of food and trained to press a lever to obtain a food pellet. The mean of response durations was less than 1.0sec and the variance was so minute that the response duration was accepted as another measure of the strength of the operant, along with the probability of occurrence in the nontreated and controlled rats. At doses of 4.0and 7.5mg, imipramine caused little effect on the rate of response; 10.0mg of the drug resulted in decrement of the response rate. Response durations increased at the minimum dose of 5.0mg, and showed a remarkable dose/response relationship. Imipramine of 15.0mg inhibited lever pressing as well as exploratory behavior in rats. The differential sensitivity of the response duration and response rate to the effect of imipramine suggests the necessity for concurrent measurement of several parameters in an operant, since it is of importance to detect that one measure is selectively affected by a given drug while the others remain unaffected. (Author abstract modified)

241378 Shibuya, Takeshi; Sakamoto, Koji; Horibe, Masahiro; Matsuda, Hiromi; Sato, Katsuhiko; Chen, Po Chung. Department of Pharmacology, Tokyo Medical College, Tokyo 160, Japan **Studies on the correlation between behavior and brain amines with psychotropic drugs.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):52P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the relationship between animal behavior and changes in brain monoamines (MA) following single administration of methamphetamine (MAPT) was reported. Catecholamine (CA) and serotonin (5-HT) in the brain were determined in male Wistar strain rats. Spontaneous motor activities in the 1mg/kg group reached a maximum at 60 min while in th 5mg/kg group showed acceleration at 30 min followed by inhibition. Brain

levels of CA decreased most significantly at 60 min in the 1mg/kg group and at 30 min in the 5mg/kg group. Brain levels of 5-HT decreased slightly at 60 min in both the 1mg/kg and 5mg/kg groups. Fluorescence intensities of CA in the nucleus locus coeruleus decreased slightly at 60 min in the 1mg/kg group and at 30, 60 min in the 6mg/kg group. Those of CA in median eminence decreased slightly at 60 min in the 1mg/kg group and at 30 min in the 5mg/kg group. It was concluded that the levels of CA or 5-HT in the rat brain correlate well with changes in spontaneous motor activity. (Author abstract modified)

241379 Nosaka, Hiroshi; Tanabe, Kyoko; Kimishima, Kenjiro. Dept. of Pharmacology, Tottori Univ. School of Medicine, Yonago 683, Japan **Effects of drugs on tremorine-induced tremor.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):53P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of various drugs on tremor induced by tremorine, which were examined in Wistar rats were reported. Studies were investigated on antitremor activities of atropine, diphenhydramine, L-5-hydroxytryptophan (L-5HTP) and L-dopa. Each drug was administered alone or in combinations with two, three and four drugs. Neither single nor combined administrations showed an inhibitory effect on tremor involving autonomic manifestation. One group given atropine, diphenhydramine and L-5HTP combined, showed a more dominant inhibitory effect on tremor and autonomic manifestation. The most dominant inhibition accompanied with fewer signs of autonomic symptoms was obtained by a combined use of atropine, diphenhydramine, L-5HTP and L-dopa. Results suggest that inhibitory mechanisms of tremor which are induced by tremorine are closely related to cholinergic, serotonergic and dopaminergic functions. (Author abstract modified)

241380 Sakurada, Shinobu; Shoji, Tooru; Kisara, Kensuke. Department of Chemical Pharmacology, Tohoku College of Pharmacy, Sendai 983, Japan **Study on head-twitches induced by intracerebrally administered tyramine in isocarboxazide-pretreated mice.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):53P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of drugs on head twitches induced by tyramine (Ty) in isocarboxazide (Iso) pretreated mice were reported. Results indicated that: p-hydroxyamphetamine in non-treated mice and Ty in Iso pretreated mice, of beta-phenylethylamines induced head twitches; injection of 5-hydroxytryptophan (5-HTP) into mice induced head twitches; when Iso Ty was injected into alpha-methyl-p-tyrosine pretreated mice, the number of head twitches increased markedly compared with Iso Ty treated group, and when Iso Ty was injected into mice sustained with p-chlorophenylalanine, the number of head twitches decreased markedly compared with the Iso/Ty treated group; the number of head twitches decreased markedly when Iso/Ty was injected into dimethothiazine pretreated mice, however the administration of Iso/Ty in haloperidol pretreated mice had no influence on head twitches; injection of Iso/Ty produced a significant increase in the dopamine level as compared with the nonpretreated group and the decrease of noradrenaline level compared with the control (Iso-saline). Although the injection of Ty only reduced the 5-hydroxytryptamine (5-HT) level, the administration of Iso/Ty produced an increase in the 5-HT level in mice. It is concluded that the head twitch response is mediated via 5-HT. (Author abstract modified)

241382 Satoh, Hisashi; Satoh, Yoshihiko; Notsu, Yoshitada; Honda, Fumio. Research Laboratories, Fujisawa Pharmaceutical Co. Ltd., Osaka 532, Japan **Cyclic 3′,5′-AMP as a possible mediator in dopaminergic stimulation-induced rotational behavior of rats lesioned unilaterally in substantia nigra.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):63P-64P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the relationship between the striatal cyclic-adenosine 3′,5′-monophosphate (cyclic AMP) and drug induced rotational response, a dopamine specific behavior was reported. Dopamine and apomorphine, reported to be dopaminergic agonists, stimulated adenylate cyclase activity in a homogenate of caudate nucleus of rats. Apomorphine elicited a rotational behavior with concomitant increase of cyclic AMP content of rats lesioned unilaterally in substantia nigra. Cyclic AMP and N6,O2′-dibutyryl cyclic AMP injected into the caudate nucleus induced rotation towards the noninjected side as did dopamine, while other nucleotides such as 5′-AMP and GTP did not. Effect of the cyclic nucleotides was potentiated with theophylline pretreatment. Rotational behavior induced by apomorphine was markedly increased with theophylline pretreatment. Rotational behavior and cyclic AMP increase induced by apomorphine were suppressed by haloperidol. These results suggest that cyclic AMP is a mediator in dopaminergic stimulation induced rotational behavior of rats. (Author abstract modified)

241397 Fujimura, Hajime; Tsurumi, Kaito; Go, Koichiro. Dpeartment of Pharmacology, Gifu University School of Medicine, Gifu 500, Japan **Behavioral effect of phthalazino-(2,3b)-phthalazine-5(14H),12(7H)-dione (L-5418).** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):92P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the behavioral effects of phthalazino-(2,3b)-phthalazine-5(14H),12(7H)-dione (L-5418) were reported. L-5418 alone did not show a hypnotic effect even at a high dose, but it potentiated barbiturate induced hypnosis in mice and rats. L-5418 inhibited markedly tonic convulsion induced by maximum electroshock, pentetrazol, Sah41-178, bemegride, pictotoxin and strychnine without inhibiting clonic convulsion in mice. It suppressed the spike discharge induced by application of penicillin to the cortical surface and by hippocampal stimulation in rabbits with acute or chronic electrode implants. On the other hand, it showed no taming effects in fighting mice and in rats with olfactory bulb ablations. Muscle relaxation or ataxia in rotarod test and inclined screen test were absent. The mode of action of L-5418 against convulsion or behavioral changes in animals was clearly different from that of hypnotics and tranquillizers. It was rather similar to the mode of action of antiepileptics such as diphenylhydantoin or carbamazepine. These results indicate L-5418 to be a potent antiepileptic of new type without hypnotic and tranquillizing actions. (Author abstract modified)

241398 Razzak, Abdul; Fujiwara, Michihiro; Ueki, Showa. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka 812, Japan **Automutilation induced by clonidine in mice.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):93P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of clonidine (2-(2-,6-dichlorophenylamino)-2-imidazoline hydrochloride) automutilation in mice were reported. Automutilation induced by colindine was not significantly altered with chronic administration of the drug, and showed no sex difference. Short-term and long-term isolation

and food deprivation of the mice had no influence on the occurrence of clonidine induced automutilation. Clonidine did not induce this behavior when the mice were placed separately in wire mesh cage, and the incidence of automutilation was decreased by 50% when the mice were given a food pellet or rod. The effects of some drugs on automutilation induced by clonidine were studied with the following results: the incidence of automutilation was increased by caffeine and theophylline the mice bit not only their own fingers of the forelimbs and hind-legs but also the skin of the thorax leaving bleeding lesions on the affected area; automutilation was not induced in mice by clonidine, 20mg/kg alone, but was induced by this drug at the same dose in mice pretreated with d-methamphetamine, caffeine and theophylline. (Author abstract modified)

241399 Iwasaki, Tsuneo; Ikeda, Yugo; Takano, Noboru. Department of Pharmacology, Research Laborotories, Chugai Pharmaceutical Co. Ltd., Tokyo 171, Japan **Pharmacological studies on 1-(3-(dimethylamino)propyl)-3-phenyl-5-methyl-1H-indazole hydrochloride (FS32) (1).** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):93P-94P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the pharmacological actions of FS32, which were compared with imipramine (IMP), were reported. FS32 showed the antireserpine and the antitetrabenazine activity, the degree of which was dose dependent. IMP exhibited a bell shaped dose response pattern. L-DOPA potentiation in spontaneous motor activity, amphetamine potentiation in self-stimulation behavior and food intake, and norepinephrine potentiation in contraction of vas deferens in vitro were also demonstrated with FS32. FS32 produced a definite suppressive effect on the isolation induced fighting episode without affecting coordinated motor activity. The same effect on the fighting behavior was shown under IMP with a slight motor incoordination. The duration of afterdischarge elicited by electrical stimulation to amygdala or hippocampus was reduced by either FS32 or IMP. FS32 was less potent than IMP in producing anticholinergic activity. The effects of FS32 on monoamine content and monoamine oxidase of the brain were found to be little, if any. Acute and subacute toxicities of FS32 were weaker than those of IMP. These findings suggest that FS32 has pharmacological properties consistent with potential clinical utility as an antidepressant drug. (Author abstract modified)

241400 Ogawa, Haruyoshi; Kuribara, Hisashi; Okuizumi, Kiyoko; Tadokoro, Sakutaro. Behavioral Research Institute, School of Medicine, Gunma University, Maebashi 371, Japan **Combined effects of methamphetamine, caffeine, diazepam, and pentobarbital on DRL performance in rats.** Japenese Journal of Pharmacology (Kyoto). 25(Suppl.):94P-95P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, the effects of the combined administration of psychotropics, methamphetamine (MA), caffeine, (CA) diazepam (DZ), pentobarbital (PB) and various combinations of these drugs (49 pairs) which were subcutaneously given to rats trained on the differential reinforcement of low rates (DRL) 20 sec schedule were reported. The single administration of each drug increased the total respondings and decreased the correct response rate as a function of the dose, thus the temporal pattern of responding was disrupted. These effects were observed most apparently in MA, and moderately in the other three drugs. When two kinds of drugs were simultaneously given to rats in various combinations, the additive effect was exhibited in about 90% of all the cases. Effects on spontaneous motor activity (SMA) after administration of the same drugs within the same dose ranges as above mentioned, differed markedly from those in the DRL performance. Increase of SMA was observed after administrations of MA, CA, and MA plus CA. Decrease of SMA was shown after DZ, PB, and and DZ plus PB. It is concluded that the behavioral effects of combined administrations of MA, CA, DZ, and PB on the DRL schedule were iargely dependent upon the doses administered together, rather than the kind of drugs. (Author abstract modified)

241401 Ishikawa, Koichi; Saito, Shoji. Department of Pharmacology, School of Medicine, Nihon University, Tokyo 173, Japan **Effects of various drugs on learning behavior of animals. 4th report. Comparison of GABA and its derivatives with adrenergic and cholinergic drugs.** Japanese Journal of Pharmacology (Kyoto). 25(Suppl.):95P-96P, 1975.

At the 48th general meeting of the Japanese Pharmacological Society, differences of the effects of gamma-aminobutyric acid (GABA), adrenaline (AD), and acetylcholine (ACh) on learning in rats were demonstrated. Male Wistar strain rats were trained in discrimination learning for 1 hr and were intraventricularly injected with GABA, AD, or ACh immediately or 60 min after each training session. The final correct responses in controls increased by about 50% in comparison with those of the first session. The response in the group injected with GABA immediately after the training increased 84%. However, AD or ACh increased the response by 52 or 55%, respectively, when the drugs were injected immediately after the training. There were significant increases in the correct responses between controls and GABA treated group, but no significant increases between the controls and AD or ACh treated group. These results show that, in the transmission of information, the GABA-ergic system may play an essential role. (Author abstract modified)

241521 Brookshire, Kenneth H.; Brackbill, Robert M. Franklin and Marshall College, Lancaster, PA 17604 **Formation and retention of conditioned taste aversions and UCS habituation.** Bulletin of the Psychonomic Society. 7(2):125-128, 1976.

Two experiments were conducted to investigate the formation and retention of conditioned taste aversions and unconditioned stimulus (UCS) habituation in rats. In the first study, rats received 10 consecutive daily injections of either apomorphine hydrochloride or sodium chloride (NaCl) followed by 4 days of saccharin solution exposure paired with apomorphine or NaCl injections. Relative consumption of saccharin solution and water during conditioning indicated that preconditioning apomorphine UCS habituation retarded acquisition of a conditioned saccharin aversion. In the second experiment, rats received 6 days of saccharin solution exposure paired with injections of either apomorphine hydrochloride or NaCl, then 10 daily injections of either apomorphine hydrochloride or NaCl, followed by 4 days of saccharin preference testing (no drug injections). Postconditioning apomorphine UCS habituation did not interfere with retention of saccharin aversion acquired in initial conditioning phase. These results show that novelty of UCS is crucial in acquisition of but not retention of conditioned taste aversions. 15 references. (Author abstract)

241546 Worsham, Elizabeth; Hamilton, Leonard W. Rutgers University, New Brunswick, NJ 08903 **The effects of septal lesions or scopolamine injections on retention of habituation to a novel environment.** Bulletin of the Psychonomic Society. 7(2):193-195, 1976.

An attempt was made to extend findings from previous studies which show that scopolamine injections or medial septal

lesions in rats disrupt the habituation of an exploratory head poke response. The effects of these manipulations on the retention of the habituated response were also examined. Exploratory responding was assessed in two 50 minute sessions separated by 10 days. The results suggest an impairment of habituation following either scopolamine injections or septal lesions during both phases 1 and 2. Septal lesions produced similar effects regardless of prior experience in the apparatus; however, injections of scopolamine resulted in different effects upon performance as a function of prior experience. Thus, in contrast to previous suggestions that the effects of these two manipulations on habituation were identical, the present study suggests that there are differences which can be observed under the appropriate testing conditions. 7 references. (Author abstract)

241668 Jones, Byron Clarence. University of Arizona **Effects of delta9-tetrahydrocannabinol on squirrel monkey incentive competition behavior. (Ph.D. dissertation).** Disseration Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-3789 HC$18.00 MF$7.50 54 p.

The efficacy of a water bottle competition paradigm in tests of behavior altering drugs was tested, and the effects of the marihuana derivative delta9-trans-tetrahydrocannabinol (delta9-THC) on drinking, social and competition behaviors in dyads of squirrel monkeys trained to compete for sweetened water were investigated. No drug related inversions in the previously determined winner/loser status of the monkeys were observed. Total competition behaviors decreased in frequency when both members received 1.0mg/kg of the drug, but increased when either the loser member or both members of low competition dyads were treated with 0.25mg/kg. Noncompetitive social behaviors increased when both animals were drugged. It is concluded that the water competition test is sensitive to the effects of behavior altering drugs and that delta9-THC produced the most salient effects when both animals were drugged. The biphasic dose effect on competition behaviors is attributed to the levels of competition evinced by the monkeys prior to drug treatment. (Journal abstract modified)

241680 Mathura, Clyde Bradman. University of Nebraska, Lincoln **Manipulation of acetylcholine levels in developing rat brain: biochemical and behavioral considerations. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-4531 HC$18.00 MF$7.50 109 p.

The effects of an early increase in acetylcholine (ACh) levels in the central nervous system of infant rats on later performance of both active avoidance and passive-avoidance tasks were investigated. The experimentally induced increase in ACh levels was studied from the perspective of age related developmental patterns of the cholinergic system in the rat brain. Litters were injected with .75mg/kg physostigmine salicylate and .025mg/kg methscopolamine hydrobromide (group I); methscopolamine hydrobromide (group II); and distilled water in like amounts to I and II (group III). The neurochemical findings show significant differences in ACh levels between groups I and III and I and II, but only in the animals injected over 15 to 28 days. The lowest level of ACh was exhibited by group I, with groups II and III following in that order. The groups injected over the 2 to 15 day period were not significantly differentiated. Both enzymes, acetylcholinesterase (AChE) and acetyltransferase (ChAc), were inversely related to ACh levels in every respect, and in a dose related fashion. These significant differences in ACh components 24 hours after systemic injections are contrasted with previous studies which demonstrated peak activities (ACh increase and AChE decrease) 30 minutes after acute injections with a return to control values after 90 minutes. Behaviorally, group I performed significantly better than II and III on both active and passive avoidance tasks. The ability of the highest dose group to perform better than controls on tasks designed to measure opposing behavioral tendencies serves to eliminate the alternative explanation of peripheral activation variables. The success in manipulating the ACh system in central nervous system of infant rats is further discussed in its relation to other putative transmitter systems. (Journal abstract modified)

241681 Thatcher, Karen Margret. Ohio State University **Cholinergic modification of DRL performance in normal rats and rats with lesions of the septum. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-3575 HC$18.00 MF$7.50 47 p.

The hypothesis that behavioral suppression requires the intact activity of an inhibitory cholinergic central nervous system mechanism was tested. A comparison was made between the effects of the administration of an anticholinesterase and a cholinergic blocker on the performance of rats using a differential reinforcement of low rates of responding (DRL) 20 second reinforcement schedule. Scopolamine impaired the performance of the DRL task, whereas physostigmine improved it. No significant effect was observed with drugs which do not pass the blood-brain barrier. The injection of physostigmine into rats with lesions of the septum produced a gradual reduction in response rates over time with a concomitant increase in DRL efficiency. Results suggest that cholinoceptive pathways arising from or passing through the septum serve a critical function in the performance of learned instrumental responses. (Journal abstract modified)

241687 Deckard, Betty Smith. University of Colorado **The genetic, biochemical and pharmacological correlates of responses to priming in mice. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-3898 HC$18.00 MF$7.50 87 p.

The genetic, biochemical, and pharmacological correlates of susceptibility to acoustic priming in mice were investigated. Genetic mechanisms are identified which influence priming induced susceptibility to audiogenic seizures as indicated by a successful program of selective breeding. The phenotype selected was not interval specific; that is, there were no significant differences between seizure severity scores of any line. Animals selected for susceptibility to priming induced seizures were not susceptible to spontaneous audiogenic seizures, and acoustic priming did not significantly affect subsequent tests of electroconvulsive seizure susceptibility in selectively bred mice. However, there were significant differences in electroconvulsive seizures between animals of the three selected lines. There were no significant differences in levels of norepinephrine, but the seizure resistant (PISR) mice had significantly lower levels of dopamine than the seizure prone (PISP) line or the unselected control line (UN), and the PISR line had significantly lower levels of serotonin than the UN line, but not than the PISP line. The effects of several psychoactive drugs on seizure susceptibility are also reported. (Journal abstract modified)

241689 Hall, Michael Eugene. University of Colorado **Variations in effect of memory altering drugs as a function of the strength of the learned response. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-3907 HC$18.00 MF$7.50 57 p.

Variations in the effects of memory altering drugs as a function of the strength of the learned response are reported. Treatment of mice with either cycloheximide (CXM) or diethyldithiocarbamate (DDC) 30 minutes before training on a passive-avoidance task altered learning in mice tested 24 hours after training. The observed alterations were dependent on the intensity of the footshock used during training. The effects of pretreatment with CXM and DDC on the acquisition of a light/dark discriminated escape task in a T-maze were dependent on the number of training trials given. It was indicated that the enhanced acquisition was due to enhanced learning of the relevance of the discriminative cue, rather than to some nonspecific enhancement of performance. Additional research indicated that, at least with DDC, the same enhancement of T-maze learning can be obtained when the drugs are administered posttraining. The results suggest that the strength of a learned response is an important variable in determining the effects of CXM and DDC on memory. When response strength is minimal, the amnesic drugs CXM and DDC act to enhance, rather than impair, the processes of learning and memory. (Journal abstract modified)

241918 Ashford, J.; Jones, B. J. Pharmacy Department, St. Luke's Hospital, Guildford, Surrey, England **The effects of intra-amygdaloid injections of 6-hydroxydopamine on avoidance responding in rats.** British Journal of Pharmacology (London). 56(3):255-261, 1976.

The effects of bilateral intra-amygdaloid injections of 6-hydroxydopamine (6-OHDA) on shuttlebox avoidance acquisition, retention, and extinction, and passive-avoidance acquisition were examined in rats. Intra-amygdaloid 6-OHDA injections produced catecholamine depletion in and around the amygdala but failed to reduce striatal dopamine concentrations. Conditioned avoidance acquisition was markedly inhibited in 6-OHDA treated rats, whereas retention and extinction were only slightly impaired. Passive-avoidance acquisition was slightly but significantly improved in rats with amygdaloid 6-OHDA lesions. Treated rats showed no motor abnormalities, they were not hypoactive in a photocell activity cage, and they performed as well as controls on a rotating rod. It is suggested that the conditioned avoidance acquisition deficit in rats with amygdaloid 6-OHDA lesions may be related to an impairment of associative learning rather than to perceptual or motor disturbances. 17 references. (Author abstract)

241927 Jaton, A. L.; Loew, D. M.; Vigouret, J. M. Biological and Medical Research Division, Sandoz, Ltd., Basel, Switzerland **CF 25-397 (9,10-didehydro-6-methyl-8beta-(2-pyridylthiomethyl)ergoline e), a new central dopamine receptor agonist.** British Journal of Pharmacology (London). 56(3):371P, 1976.

The action of CF25-397 (9,10-didehydro-6-methyl-8beta-(2-pyridylthiomethyl)ergoline), a new, nonpeptide ergot derivative which seems to exert central dopamine like actions that differ from the effects of bromocriptin or L-dopa and appears to be more selective, is described. Results of experiments with rats suggest that CF25-397 may provide a new and more selective treatment for patients suffering from extrapyramidal disorders. 3 references.

241932 File, Sandra E. Department of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Are central cholinergic pathways involved in the habituation of exploration and distraction?** British Journal of Pharmacology (London). 56(3):378P-379P, 1976.

The involvement of muscarinic systems in the brain in long-term habituation of exploration and distraction was tested in rats injected with scopolamine. Experiments with rats in holeboards, with observations made of head dipping, and experiments with rats and tonal distractions provide no support for the suggestion that central muscarinic systems are essential for habituation of exploration or distraction. 3 references.

241979 Evans, Jane P. M.; Grahame-Smith, D. G.; Green, A. R.; Tordoff, Ann F. C. MRC Unit, Radcliffe Infirmary, Oxford OX2 6HE, England **Electroconvulsive shock increases the behavioural responses of rats to brain 5-hydroxytryptamine accumulation and central nervous system stimulant drugs.** British Journal of Pharmacology (London). 56(2):193-199, 1976.

The effects of electroconvulsive shock (ECS) on rat brain 5-hydroxytryptamine (5-HT) synthesis and metabolism are examined. A single ECS increased the concentration of rat brain 5-hydroxyindoleactic acid (5-HIAA) but did not alter brain 5-HT or tryptophan concentrations 3 hr later. A single ECS decreased 5-HT synthesis 3 hr and 6 hr later. Synthesis was back to normal after 24 hr. The results of further experiments indicate that: a single electroshock does not alter 5-HT functional activity; 5-HT synthesis and accumulation of 5-HT following tranylcypromine and L-tryptophan are not altered by ECS; altered postsynaptic responses to 5-HT receptor stimulation are found; repeated ECS enhances locomotor activity following tranylcypromine and L-dopa but does not alter brain noradrenaline or dopamine concentrations; the latent period before a pentylenetetrazol induced convulsion is shortened by repeated ECS. It is concluded that following repeated ECS there appears to be increased neuronal sensitivity to certain stimuli producing centrally mediated behavioral stimulation. This is discussed in relation to the mechanism by which electroconsulsive therapy produces its therapeutic effects. 22 references. (Author abstract modified)

241994 Ono, Joyce Kazuyo. University of Illinois, Urbana-Champaign **Psychopharmacological characterization of a drug-induced grooming behavior in the cricket, Acheta domesticus (insecta, orthoptera). (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-6896 HC$18.00 MF$7.50 97 p.

The neurochemical and neuroanatomical basis of a drug inducible cercal/abdominal grooming behavior was investigated in the domestic cricket Acheta domesticus with the hope of characterizing a preparation in which the neurophysiological and neurochemical basis of a behavior could be elucidated. The effects of several agonistic and antagonistic monoamine affecting drugs and the putative monoamine neurotransmitter, dopamine (DA), norepinephrine (NE), and 5-hdroxytryptamine (5HT) on the grooming behavior were investigated. Only a few of the drugs tested, ergotamine, haloperidol, cocaine, and iproniazide affected the cleaning behavior when administered alone. Ergotamine, haloperidol, cocaine and pyrogallol affected desipramine (DMI) induced grooming behavior. Monoamine depletion by reserpine led to a diminishing of the DM induced cleaning level, however, depletion by parachlorophenylalanine (PCPA) and alpha-methyl-meta-tyrosine (aMMT) did not lead to a decrease in the cleaning level. These findings in conjunction with the lack of response to many other monoamine affecting drugs suggest that the cleaning behavior is not the result of DMI affecting the biogenic amines, 5HT, DA or NE. The drug inducible behavior did not appear to be the result of increasing the level of general excitation in the cricket central nervous system (CNS), for a pulse of hyperactivity inducing stimuli did not increase the

level of cleaning induced by a suboptimal dose of DMI. (Journal abstract modified)

242205 Kameyama, Tsutomu; Shigehisa, Tsuyoshi; Nabeshima, Toshitaka. Dept. of Chemical Pharmacology, Faculty of Pharmaceutical Sciences, Meijo University, Tempaku-Ku, Nagoya 468, Japan **Correlation between the 5-hydroxytryptamine contents in the brain and degrees of sensory, and locomotor activities in the rat.** Japanese Journal of Pharmacology (Kyoto). 25(6):784-787, 1975.

The way in which brain 5-hydroxytryptamine (5-HT) may have a specific measurable correlation to degrees of sensory and locomotor activities was investigated in Sprague-Dawley rats. For each animal, auditory threshold, locomotor activity, and 5-HT content were measured. Correlation coefficients were calculated between 5-HT content, auditory threshold, bar-press speed, ambulation, rearing, defecation and grooming scores. Results reveal a significant positive relationship between telencephalic 5-HT and auditory threshold, and nontelencephalic 5-HT and ambulation. There was also a significant negative correlation between telencephalic/nontelencephal ic ratio of 5-HT and defecation. To demonstrate further that telencephalic 5-HT is negatively correlated with auditory sensitivity, rats pretreated with DL-p-chlorophenylalanine (pCPA) were subjected to threshold determination. Findings support the hypothesis that the greater the content of 5-HT in the telencephalon, the less the sensory activity. 7 references.

242732 Benesova, O. Institute of Pharmacology, Medical Faculty of Hygiene, Charles University, Prague, Czechoslovakia **Effect of 10 days reserpine or apomorphine administration on sleep cycles in rats.** Pharmacology, Biochemistry and Behavior. 4(2):119-122, 1976.

The duration of sleep/wakefulness periods and sleep cycles was investigated electroencephalographically and electromylographically in rats during 5 hr trials after repeated administration of two depressant drugs, reserpine and apomorphine. Ten days administration of reserpine at a dose of 0.05mg/day subcutaneously decreased the duration of both slow wave and paradoxical sleep, whereas apomorphine had no effect on sleep duration or occurrence of sleep phases in either the low dose or in the high dose of 0.6mg/kg/day. This finding might be correlated with previously found differences in catecholamine levels in the brain in the same model experiments. 18 references. (Author abstract modified)

242733 Palfai, Tibor; Kurtz, Perry. Psychology Laboratories, M-15 Lambreth Lane, Syracuse University, Syracuse, NY 13210 **Dose-related effects of Metrazol on retention and EEG.** Pharmacology, Biochemistry and Behavior. 4(2):123-127, 1976.

The effects of various dose levels of Metrazol on retention and electrocorticogram (ECoG) were investigated. Mice given a subconvulsive 30mg/kg or a convulsive 50mg/kg dose of Metrazol 15 min before reversal training in a discriminated escape learning task showed retention impairment of reversal training retention. Lower dose levels (5 or 10mg/kg) had no effect. The 30mg/kg dose produced asymmetrical dissociation. The convulsive dose (50mg/kg), previously reported to result in symmetrical dissociation, produced ECoG changes that were still evident 15 min following the injection; i.e.,at the time when training or testing usually took place. With lower doses (10 or 30mg/kg), no apparent ECoG effects were observed at this interval. The implications of the findings were discussed with respect to the state-dependent learning hypothesis. 11 references. (Author abstract)

242737 Jarbe, Torbjorn U. C.; Johansson, Jan O. University of Uppsala, Dept of Psychology, Tradgardsgatan 20, S-752 20 Uppsala, Sweden **Drug discrimination in rats: effects of mixtures of ditran and cholinesterase inhibitors.** Pharmacology, Biochemistry and Behavior. 4(2):151-157, 1976.

Groups of rats were trained in a T-shaped maze to discriminate the effects produced by intraperitoneal injections of ditran, either when given singly, or when combined with the acetylcholinesterase inhibitors neostigmine or physostigmine, from the nondrug condition (saline). The results from this state-dependency (StD) model indicated that acquisition of the drug discrimination was similar for the four groups of rats. After drug discrimination was established the rats were tested with various drug combinations. Physostigmine challenge reversed drug discrimination among rats trained with ditran solely or the ditran plus neostigmine combination. There was no antagonism among the ditran plus physostigmine trained rats. Involvement of the central nervous system is implicated since test results of physostigmine treated mice also increased with ditran. It is concluded that this study indicates the usefulness of employing both training and transfer test procedures when evaluating antagonism in this StD model. 31 references. (Author abstract)

242739 Ksir, Charles. Dept. of Psychology, University of Wyoming, Laramie, WY 82071 **Rate dependent drug effects: possible state dependency.** Pharmacology, Biochemistry and Behavior. 4(2):165-168, 1976.

The phenomenon of rate dependency, of practical importance to behavioral pharmacologists because it means that most drugs cannot be classified as enhancers or diminishers of responding, is examined. Of six rats given an extensive experience responding on a fixed-interval reinforcement schedule after injections of 1mg/kg d-amphetamine, three showed significant rate dependent changes in responding when presession saline was substituted for d-amphetamine. Low rates were increased and high rates decreased by the change from d-amphetamine to saline, a result commonly found when d-amphetamine is first introduced. This indicates that rate dependent changes in fixed-interval responding may be state-dependent phenomena. 15 references. (Author abstract modified)

242742 Tucker, Alan; Gibbs, Marie. Dept. of Psychology, La Trobe University, Bundoora, 3083, Australia **Cycloheximide-induced amnesia for taste aversion memory in rats.** Pharmacology, Biochemistry and Behavior. 4(2):181-184, 1976.

The effects of a protein synthesis inhibitor, cycloheximide (CXM), on saccharin aversion memory in the rat are reported. Male hooded rats were conditioned in one trial to avoid saccharin by pairing saccharin drinking with an intragastric injection of lithium chloride. A 24 hr water/saccharin preference test showed that conditioned rats exhibited a very low preference for saccharin whereas rats injected intraventricularly with CXM 5, 7, or 9 hr before training exhibited a greatly increased saccharin preference which differed significantly from sodium chloride injected controls. This 24 hr amnesia was found to be dependent upon the time of administration of CXM, since injection at 1, 3, or 17 hr before training did not confer amnesia. The nature of the task, a control measure, and a control experiment indicate that the CXM induced change in saccharin preference at 24 hr is not due to a CXM induced aversion, nor a loss in drinking ability, nor an inability to retrieve information while under the influence of CXM. 18 references. (Author abstract modified)

242743 Quadagno, David M.; Albelda, Steven M.; McGill, Thomas E.; Kaplan, Lawrence J. Dept. of Psychology, Williams College, Williamstown, MA 01267 **Intracranial cycloheximide: effect on male mouse sexual behavior and plasma testosterone.** Pharmacology, Biochemistry and Behavior. 4(2):185-189, 1976.

The effects of cycloheximide (CXM) infusions on sexual behavior and plasma testosterone levels in intact male mice are examined. Experimental findings suggest that CXM acts primarily by inhibiting sexual arousal rather than sexual performance. The inhibition of sexual behavior was not observed when the males were tested 84 hr after treatment. After exposure to an estrous female, plasma testosterone levels were measured in males with preoptic area infusions of CXM or saline vehicle. No significant difference was found, but both groups had significantly higher levels of plasma testosterone than males not exposed to estrous females. It is suggested that the interference with sexual behavior by CXM was not due to interference with the neuroendocrine mechanisms controlling blood androgen levels, but due to CXM acting directly on the neural circuits controlling sexual responsiveness. 19 references. (Author abstract modified)

05 TOXICOLOGY AND SIDE EFFECTS

238807 Rosenkrantz, Harris; Hayden, David; Braude, Monique C. Mason Research Institute, Worcester, MA 01608 **Inhalation toxicity of Turkish marihuana, cannabichromene (CBCH) and cannabidiol (CBD) in rats.** Federation Proceedings. 35(3):643, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the inhalation toxicity of Turkish marihuana, cannabichromene (CHCH) and cannabidiol (CBD) in rats was reported. Delayed central nervous system (CNS) inhibition followed by tolerance occurred for all cannabinoids, but CNS stimulation was absent. A dose related delayed lethal toxicity occurred for Turkish marihuana; no rats died in CBD, CBCH or placebo groups. Dose related decreases in male exploratory activity and rate of growth were observed for all cannabinoids but food and water consumption increased. Relative organ weights at the higher doses were elevated: male brain, lung, kidney and heart; female kidney, liver and heart for Turkish marihuana and 10-27% for CBCH brain, kidney, liver and testes. CBD and CBCH alone or together induced seminiferous tubule degeneration in a dose related manner. Acute inhalation median lethal dose values for Turkish marihuana, CBD or CBCH were estimated to be 10, 34 and 32mg/kg, respectively. The results indicate that CBD and CBCH contribute toxicity to marihuana use. (Journal abstract modified)

239041 Chritensen, Sten. Dept. of Pharmacology, Univ. of Copenhagen, 20 Juliane Mariesvej, DK-2100 Copenhagen, Denmark **Effect of antidiuretic drugs in rats with lithium-induced polyuria.** Acta Pharmacologica et Toxicologica (Kobenhavn). 38(2):81-89, 1976.

The effect of various antidiuretic drugs was studied in rats with lithium induced polyuria. Constant polyuria was induced in male Wistar rats by administration of lithium chloride in the food for 2-3 months before the experiments. Bodyweight, food consumption, urine volume, and osmolality were recorded daily. After a 7 days control period, drugs were administered once or twice daily for 7 days. Bendroflumethiazide produced a reversible, dose dependent antidiuretic response as indicated by a decrease in free water clearance. After 10mg/kg, negative free water clearance was induced and the urine flow was reduced to one third. Diazoxide, chlorpropamide and carbamazepine did not significantly affect urine volume or osmolality at dose levels producing no effects on food consumption or body weight. The antidiuretic response to a thiazide diuretic and lack of response to drugs known to have antidiuretic action in pituitary diabetes insipidus, lend support for the nephrogenic basis of the concentration defect induced by lithium. 25 references. (Author abstract)

239043 Alhava, Eeva. Dept. of Pharmacology, Univ. of Helsinki-17, Siltavuorenpenger 10, SF-00170 Helsinki-17, Finland **Effects of catecholamine receptor blocking agents on toxicity and thermal responses induced by amphetamine isomers in adult and developing mice.** Acta Pharmacologica et Toxicologica (Kobenhavn). 38(2):161-173, 1976.

The effects of catecholamine receptor blocking agents on toxicity and thermal responses induced by amphetamine isomers in adult and developing mice were examined. The toxicity of d-amphetamine was greater than that of l-amphetamine in adult mice; neither isomer was toxic to developing mice. Both isomers of amphetamine induced a dose dependent hyperthermia in adults. Ten mg/kg of d-amphetamine increased the temperature of developing mice, while 50mg/kg of both isomers was markedly hypothermic; p-OH-amphetamine was not lethal and lacked the thermal effect in adult and developing mice. Phenoxybenzamine completely protected adult mice against the toxicity of 50mg/kg of d-amphetamine. It also attenuated the d-amphetamine-induced hyperthermia in adult as well as hypothermia in developing mice. Propranolol partially protected adult mice against d-amphetamine toxicity and clearly antagonized the hyperthermia. In combination with propranolol, d-amphetamine was toxic to developing mice and potentiated the hypothermia. Metoclopramide partially protected adult mice against d-amphetamine toxicity and diminished the hyperthermia. In developing mice, metoclopramide increased d-amphetamine toxicity, but decreased the hypothermia. 25 references. (Author abstract modified)

239046 Christensen, Sten. Dept. of Pharmacology, University of Copenhagen, 20 Juliane Maries Vej, DK-2100 Copenhagen, Denmark **Acute and chronic effects of vasopressin in rats with lithium-polyuria.** Acta Pharmacologica et Toxicologica (Kobenhavn). 38(3):241-253, 1976.

The acute and chronic effects of vasopressin were studied in rats with polyuria due to long-term administration of lithium. In anaesthetized, water loaded animals, lithium pretreatment producing severe polyuria inhibited the response to physiological doses of arginine vasopressin by 95% as glucose drinking. The percent inhibition of vasopressin response was somewhat reduced by increasing the dose of the hormone. There was no difference in osmolality of renal medullary tissue from lithium polyuric and glucose polydipsic rats when determined at the end of the experiments. Daily subcutaneous injections of vasopressin to conscious animals, kept in metabolic cages, caused a significant antidiuretic response in rats with severe lithium polyuria and almost completely reversed the urine flow in animals with partial concentration defect. The results are compatible with the view that lithium polyuria in rats is due to impairment of the renal response to vasopressin. Being virtually unresponsive to physiological doses of vasopressin, however, the polyuria can be partly reversed by increasing the level of circulating hormone. 20 references. (Author abstract)

239089 Arseni, C.; Nereantiu, Florica; Nicolescu, P.; Horvath, Lenke. Clinica de Neurochirurgie, Spitalul 'Dr. Gh.

Marinescu', Str. Berceni 10, Bucharest, Rumania **Encephalopathy subsequent to accidental poisoning with chlorpromazine.** European Neurology (Basel). 14(1):29-38, 1976.

A cerebral biopsy performed in an infant 9 months after accidental poisoning with chlorpromazine was studied. Light microscopy disclosed necrosing encephalopathy, while electron microscopy showed neuronal, glial, myelinic and vascular lesions. Findings suggest that the various neurologic syndromes appearing in cases of prolonged treatment with neuroleptic drugs and persisting after cessation of therapy would be due to consequent occurrence, in specific areas, of some irreversible cerebral lesions. 15 references. (Author abstract)

239091 Harri, Mikko N. E. Zoophysiological Lab., Dept. of Zoology, Univ. of Turku, SF-20500 Turku 50, Finland **Amphetamine toxicity in temperature-acclimatised mice.** Acta Pharmacologica et Toxicologica (Kobenhavn). 38(1):1-9, 1976.

D-Amphetamine toxicity was tested in mice previously acclimatized to 5, 21 and 31 degrees. When the measurements were carried out at 21 degrees, mice acclimatized to lower ambient temperatures were more sensitive to amphetamine than those acclimatized to higher ones. However, when measured at 14 degrees, toxicity was similar for 5 degrees and for 21 degrees acclimatized mice, while it was greater for 31 degrees acclimatized mice. Aggregation increased amphetamine toxicity more the greater the toxicity had been in isolated animals. The body temperature of mice under the influence of amphetamine was inversely related to the previous temperature of acclimatization, and it was always lower at 14 degrees than at 21 degrees. Aggregation did not influence the hyperthermic effect of amphetamine, while it tended to decrease the hypothermia caused by the drug. The differences in amphetamine toxicity between animals acclimatized to different temperatures can be accounted for by differences in relation to the experimental situation, rather that by differences in susceptibility to the drug. 17 references. (Author abstract)

240205 Nikolova, M.; Daleva, L.; Nikolov, R. Chemical and Pharmaceutical Research Institute, Zhelyo Voivoda l-a, Sofia, Bulgaria **Study of development of tolerance to and barbiturate-like physical dependence on the tranquillizer Tempidon.** Agressologie (Paris). 16(C):43-47, 1975.

Development of tolerance to and barbiturate-like physical dependence on the tranquillizer Tempidon (2,2,6,6-tetramethyl-piperidon-4-toluene-p-sulphonate) were studied in rats and dogs. The following tests were used for establishing tolerance: acute toxicity, potentiation of hexobarbital, and orientation reflex. Hydroxyzine, chlordiazepoxide, and meprobamate were used as controls. The results indicate that long-term use of Tempidon in doses of one tenths of the median lethal dose does not induce tolerance to its toxic action and central depressive effect. Chlordiazepoxide and meprobamate cause an alcohol/barbiturate type of physical dependence. 11 reference. (Author abstract modified)

241249 Jarvis, J. A. E.; Magos, L. MRC Toxicology Unit, Medical Research Council Lab., Woodmansterne Rd., Carshalton, Surrey, SM5 4EF, England **Effects of diethyldithiocarbamate on the catabolism of tyrosine in the rat brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 292(3):295-298, 1976.

A dose of 500mg/kg sodium diethyldithiocarbamate (DDC) and trace quantities of uniformly labeled 14C-tyrosine were administered simultaneously to determine the effect of DDC on catabolism of tyrosine. Thirty minutes later, total radioactivity, the concentration and the specific activity of free tyrosine were increased both in plasma and in the brain by 40% compared with untreated rats. The incorporation of 15C from 14C-tyrosine into glutamine/glutamate was 80% less in the brain 30 min after DDC. The exhalation of 14CO2 was depressed by 80% in the first hour after DDC. When 14C-tyrosine was given 3.5h after DDC the only differences between experimental and control rats were the increased incorporation of 14C into the glutamine/glutamate and aspartate fractions and the increased exhalation of 14C02. It is concluded that DDC, an inhibitor of dopamine hydroxylase, also interferes with the major catabolic pathway of tyrosine. 15 references. (Author abstract modified)

241934 Anlezark, G. M; Marsden, C. D.; Meldrum, B. S. Department of Neurology, Institute of Psychiatry, London SE5 8AF, England **A primate model of acute dystonic reaction to neuroleptics.** British Journal of Pharmacology (London). 56(3):381P, 1976.

A primate model of acute dystonic reaction to neuroleptics is described, which was discovered during the course of testing haloperidol and pimozide in the photosensitive baboon, Papic papio. A possible explanation of dystonic reactions to neuroleptic drugs is advanced. It is suggested that the dopamine release that they cause activates dopaminergic synapses not blocked by the neuroleptics. Pretreatment with reserpine and alpha-methyl-p-tyrosine decreased the severity of the dystonic responses to haloperidol and delayed its onset. 3 references.

241982 Arefolov, V. A.; Pidevich, I. N.; Panasyuk, L. V.; Firsov, V. K. Laboratoriya farmakologii nervnoy sistemy Instituta farmakologii AMN SSSR, Moscow, U.S.S.R. **/Pharmacological analysis of some adrenomimetic effects of serotonin./** Farmakologicheskiy analiz nekotorykh adrenomimeticheskikh effektov serotonina. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 80(11):45-48, 1975.

The effects of antagonists of serotonin, the sympatholytic bretilium, the alpha-adrenolytic droperidol, and imipramine on the contractions of isolated rat vas deferens induced by serotonin were tested. Reductions of the isolated sperm flow, caused by serotonin, were not connected with direct excitation of serotonin and adrenoreactive structures. They were explained by the release of catecholamines from the nerve endings. 10 references. (Journal abstract modified)

241983 Dil'man, V. M.; Anisimov, V. N. Instituta onkologii imeni N. N. Petrova Ministerstva zdravookhraneniya SSSR, Leningrad, U.S.S.R. **/Increase in hypothalamic sensitivity to the inhibitory action of estrogens caused by the use of L-dopa, Dilantin, epithalamin, and phenoformin in old rats./** Povysheniye chuvstvitel'nosti gipotalamusa k ingibiruyuschemu deystviyu estrogenov, vyzvannoye primeneniyem L-DOPA, difenina, epitalamina i fenformina u starykh krys. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 80(11):96-98, 1975.

A total of 484 white rats was studied for reactions to L-dopa, Dilantin (diphenylhydantoin), epithalamin, or phenoformin and estrogens. Daily treatment of hemicastrated young rats with 0.57 microgram of stilbestrol inhibited compensatory ovarian hypertrophy by 48% in 3-month-old animals, but by only 3% in 18-month-old animals. Administration of the investigated drugs with the same dose of estrogen to old rats suppressed compensatory ovarian hypertrophy by 65-98%. L-dopa and epithalamin were effective when introduced into the third cerebral ventricle. A functional nature of the age changes in hypothalamic sensitivity to the estrogen action is postulated. 15 references. (Journal abstract modified)

06 METHODS DEVELOPMENT

238683 Billings, R. E.; Murphy, P. J.; Bellamy, G.; McMahon, R. E.; Ashmore, J. Department of Pharmacology, Indiana Univ. School of Medicine, Indianapolis, IN 46206 **The aromatic hydroxylation of amphetamine with rat liver microsomes, perfused liver and isolated hepatocytes.** Federation Proceedings. 35(3):243, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a simplified sensitive method for the determination of p-hydroxyamphetamine (HO-A) was reported. The method involves conversion of the extracted HO-A to the pentafluoropropionate followed by gas chromatographic (GC) analysis using an electron capture detector. In 2 hours the perfused liver metabolizes about 50% of the administered A to HO-A. Most of the HO-A was further metabolized by conjugation. Isolated liver cells hydroxylate A and conjugate HO-A at a rate comparable to that of the perfused liver. With the isolated cells the rates of hydroxylation of d-A and l-A are the same at concentrations of 20-200 microM. The hydroxylation reaction was inhibited by such typical microsomal oxygenase inhibitors as SKF-525A as well as by iprindole. The rate could not be increased by induction of cytochrome P450. (Journal abstract modified)

239683 Lewi, P. J. Research Laboratories, Janssen Pharmaceutica N. V., B-2340 Beerse, Belgium **Spectral maps of the Liege-physiognomies of the neuroleptics.** Pharmakopsychiatrie Neuro-psychopharmakologie (Stuttgart). 8(6):375-379, 1975.

Spectral mapping is described as a classification technique that has been applied to the Liege physiognomies of the neuroleptics. The method makes use of a special projection that separates potency from spectral information. Principal component analysis revealed a dominant component resembling a bipolar incisive/sedative scale. A second antimanic/antiautistic scale is apparent in the revised Liege physiognomie. Spectral mapping allows comparison of observations on neuroleptics in different frames of reference and from different methodologies (e.g.,clinical and pharmacological). 14 references. (Author abstract)

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

242527 Pyszko, Jan. Regionalkrankenhaus, CH-2800 Delemont, Switzerland **/Clinical research with Demetrin in surgery patients./** Klinische Untersuchungen mit Demetrin bei chirurgischen Patienten. Medizinische Welt (Stuttgart). 25(22):1004-1006, 1974.

The efficacy of Demetrin (prazepam) as a tranquilizer for surgical patients was investigated. The dosage was proportioned to patient weight and psychological condition. The findings show the optimal dosage ranging from 0.45mg/kg to 0.55mg/kg. Age is not a factor. A sleep conducive effect is obtained with a day dosage of 0.30mg/kg complemented by a 0.40mg/kg evening dosage. Preoperative individual doses ranging between 0.40mg/kg to 0.45mg/kg 10 to 15 hours prior to anesthetic onset are especially favorable. Demetrin possibly exercises an effect on the smooth musculature as well. The three main uses of Demetrin in surgically treated patients are: 1) preoperatively, 2) postoperatively, and 3) physiotherapeutically. (Author abstract modified)

08 DRUG TRIALS IN SCHIZOPHRENIA

238864 Woggon, B.; Angst, J.; Margoses, Nadja. Psychiatrische Universitats-Klinik, CH-8000 Zurich, Switzerland **/Present state of long-term neuroleptic treatment of schizophrenia./** Gegenwartiger Stand der neuroleptischen Langzeitbehandlung der Schizophrenie. Nervenarzt (Berlin). 46(11):611-616, 1975.

Long-term neuroleptic treatment of schizophrenia is discussed. Studies are cited which suggest that acute forms of schizophrenia are increasing as compared to chronic forms, and that only one third are successfully cured, the majority requiring long-term care. Ambulatory neuroleptic treatment of schizophrenia is observed to facilitate the patient's reintegration into society and, through the lowered risk of rehospitalization, to stablize family and interpersonal relationships. Questions of effective dosage and side-effects of various neuroleptics are discussed. Of the neuroleptics given by injection, fluphenazine enanthate and fluphenazine decanoate are most commonly used. The only oral neuroleptic with long-term effectiveness, up to one week per dose, is penfluridol. 60 references.

238975 Haslam, M. T.; Bromham, B. M.; Schiff, A. A. Clifton Hospital, York, England **A comparative trial of fluphenazine decanoate and flupenthixol decanoate.** Acta Psychiatrica Scandinavica (Kobenhavn). 51(2):92-100, 1975.

A double-blind crossover study is reported which compares the antipsychotic properties and the side-effects of depot flupenthixol with fluphenazine decanoate in chronic schizophrenic inpatients. Special emphasis was laid on examining changes in the target symptoms of apathy/anergia and depression in which flupenthixol has been claimed to be particularly effective. No significant differences were found between treatments on schizophrenic symptoms, or in extrapyramidal side-effects produced by equipotent doses of the two drugs. Reasons for the essentially negative results are discussed against a background review of earlier optimistic studies of flupenthixol. 28 references. (Author abstract)

238996 Johnson, D. A. W.; Malik, N. A. Crumpsall Hospital, Manchester M8 6RB, England **A double-blind comparison of fluphenazine decanoate and flupenthixol decanoate in the treatment of acute schizophrenia.** Acta Psychiatrica Scandinavica (Kobenhavn). 51(4):257-267, 1975.

A double-blind comparison of fluphenazine decanoate and flupenthixol decanoate in 40 consecutive admissions showed no difference in antipsychotic effect or extrapyramidal side-effects after 56 days. However, the trial identified a differential effect of the drugs on mood: flupenthixol decanoate had an elating effect that was most marked during the week following injection; fluphenazine decanoate tended to lower mood. The results suggest that in acute schizophrenia, fluphenazine decanoate is a more appropriate drug in elated or acutely disturbed patients, but that in patients with a lowered mood or a history of depression, flupenthixol decanoate is more appropriate. It was emphasized that these mood changes were observed in patients with acute schizophrenia and that extrapolation from these results to maintenance therapy of chronic relapsing schizophrenia should only be made with caution. Analyses of covariance showed a significant positive correlation between the incidence of extrapyramidal side-effects and duration of illness. 11 references. (Author abstract modified)

239023 Gerlach, Jes; Kramp, Peter; Kristjansen, Palle; Lauritsen, Bent; Luhdorf, Kurt; Munkvad, Ib. Dept. E, St. Hans Hospital, DK-4000 Roskilde, Denmark **Peroral and parenteral administration of long-acting neuroleptics: a double-blind study of penfluridol compared to flupenthixol decanoate in the treatment of schizophrenia.** Acta Psychiatrica Scandinavica (Kobenhavn). 52(2):132-144, 1975.

A total of 56 schizophrenic patients completed a double-blind study of two long-acting neuroleptics, penfluridol (peroral) and flupenthixol decanoate (parenteral). Half of the patients were on maintenance therapy of flupenthixol prior to the study, the other half on penfluridol. Patients in the two main groups were randomly divided into two further groups, one continuing the medication unchanged, the other changing to the alternative drug. It was possible to make a sudden switch from penfluridol to flupenthixol decanoate and vice versa without any significant change in the condition of the patient. The same dosage (in 70% of the patients from 40 to 80mg) of penfluridol was used per week as was employed for flupenthixol decanoate per fortnight. Changes in the intensity of the symptoms (total Brief Psychiatric Rating Scale (BPRS) score) were more pronounced in the preliminary period (during unchanged treatment) than on changed medication in the blind period. Both drugs induced approximately the same degree of akathisia, Parkinsonism and autonomic side-effects. The practical consequences of equipotent therapeutic effect of a peroral and parenteral long-acting neuroleptic are briefly discussed. 19 references. (Author abstract modified)

239823 Floru, L.; Heinrich, K.; Wittek, F. Rheinisches Landeskrankenhaus, University of Dusseldorf, Bergische Landstr. 2, D-4 Dusseldorf 12, Germany **The problem of post-psychotic schizophrenic depressions and their pharmacological induction: long-term studies with fluspirilene and penfluridol and single-blind trial with fluphenazine-decanoate and flupenthixol-decanoate.** International Pharmacopsychiatry (Basel). 10(4):230-239, 1975.

The historical aspects, as well as the various etiological and clinical factors which contribute to the so called pharmacogenically induced depressions during treatment by means of neuroleptics generally, and long-term neuroleptics especially, are discussed. An open study of 161 schizophrenic patients treated by means of fluspirilene and 123 patients treated by means of penfluridol is described. A single blind trial on 48 patients, by means of fluphenazine decanoate and flupenthixol decanoate, which compares the possible depression inducing or antidepressant activity of the above drugs, is presented. The criteria for evaluating drug induced depressions and their two clinical types are discussed. 64 references. (Author abstract)

239931 Meltzer, Herbert Y.; Fang, Victor S. Dept. of Psychiatry, Univ. of Chicago, Pritzker School of Medicine, 950 E. 59th St., Chicago, IL 60637 **The effect of neuroleptics on serum prolactin in schizophrenic patients.** Archives of General Psychiatry. 33(3):279-286, 1976.

Serum prolactin levels were studied before and during long-term administration of phenothiazines on a twice daily schedule to 27 newly-admitted schizophrenic patients. An increase in serum prolactin is believed to be a reflection of inhibition of dopamine receptors in the hypothalamo/pituitary axis. By 72 hours after the initiation of treatment, all 27 patients had persistently elevated serum levels averaging 3.2fold and 3.8fold in men and women, respectively. Serum prolactin levels remained elevated during the 1 to 3 month period subjects were studied, suggesting there was no tolerance to this effect of phenothiazines. Serum prolactin levels tended to be higher with thioridazine than on equivalent doses of chlorpromazine or trifluoperazine hydrochloride. There was some evidence that the magnitude of the serum prolactin elevation correlated with clinical response. After cessation of phenothiazines, serum prolactin levels rapidly reverted to normal within 48 to 96 hours. 40 references. (Author abstract modified)

239933 Janowsky, David S.; Davis, John M. Dept. of Psychiatry, School of Medicine, Univ. of California at San Diego, La Jolla, CA 92037 **Methylphenidate, dextroamphetamine, and levamfetamine: effects on schizophrenic symptoms.** Archives of General Psychiatry. 33(3):304-308, 1976.

The relative psychosis activating properties of methylphenidate, dextroamphetamine sulfate, and levamfetamine succinate in actively ill schizophrenic patients were investigated. The three drugs were administered in equimolar doses. Methylphenidate was a more effective activator of symptoms than dextroamphetamine, which in turn was more effective than levamfetamine. Levodopa (L-dopa) given orally also reportedly produces a temporary worsening of schizophrenic symptoms. While these findings augment a body of information suggesting that dopamine and norepinephrine may play a role in the activation of schizophrenic symptoms, findings with methylphenidate (reportedly weak in eliciting stereotyped behavior in rats) and a review of the literature indicate complexities that remain to be resolved. There is some utility of the procedure for differential diagnosis and selective therapy, but this is still of occasional and limited potential. 23 references. (Author abstract modified)

240218 Ruther, E.; Schilkrut, R.; Ackenheil, M.; Eben, E.; Hippius, H. Psychiatrische Klinik, Universitat Munchen, 8 Munich 2, Nussbaumstr. 7, Germany **Clinical and biochemical parameters during neuroleptic treatment: I. Investigations with haloperidol.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 9(1):33-36, 1976.

Clinical and biochemical parameters were examined in 26 patients with a paranoid/hallucinatory syndrome who were treated with a fixed daily dose of haloperidol. Psychopathological symptoms and Parkinsonism were studied before and during the treatment. Homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA) concentrations in cerebrospinal fluid (CSF) were determined immediately before and after 5 or 15 days of treatment. After 5 days of treatment, a slight effect was observed on psychotic symptoms and on the extrapyramidal motor system, as well as an elevation of HVA and 5-HIAA concentrations in CSF. After 15 days of treatment, the extrapyramidal and antipsychotic effects were significant, but the rise of HVA was smaller than after 5 days of treatment; 5-HIAA remained unchanged. These different time courses of the neuroleptic effects on psychopathological symptoms, on the extrapyramidal system and on monoamine metabolites concentration in CSF are interpreted as a development of drug tolerance in relation to the biochemical parameters. 24 references. (Author abstract)

240663 Carney, M. W. P. Northwick Park Hospital, Watford Rd., Harrow, Middlesex HA1 3UJ, England **Fluphenazine decanoate.** Lancet (London). 1(7958):546, 1976.

Advantages of slow release injections in the maintenance treatment of schizophrenia are discussed. Community treatment methods based upon chemotherapy are recommended. Evidence of many schizophrenics now maintained on depot fluphenazine and flupenthixol, who are reintegrated and resettled in society, is cited to demonstrate the value of such treatment.

240709 Peters, U. H. 65 Mainz, Langenbeckstr. 1, Germany **/Long-term treatment of schizophrenia./** Langzeittherapie der Schizophrenie. Medizinische Welt (Stuttgart). 26(25):1234-1936, 1975.

Requirements for long-term psychotherapeutic treatment of schizophrenia are outlined. Schizophrenia is defined as an inability to adequately receive or process information. The psychopharmacological treatment of schizophrenia is also described. Data from several research studies are cited, and a placebo/treatment experiment conducted by Hogarty, Goldberg, Schooler, and Ulrich which showed that 80% of 374 previously discharged patients had to be readmitted within 2 years is evaluated. Mere psychotherapy is felt to exacerbate the patient's condition, and it is suggested that drug therapy is also necessary. 4 references.

240850 Sanchez T. E.; Ning, J. Li; Nunez A. H.; Medina, E. University of San Marcos, Peru **/Treatment of acute schizophrenia with sulphoridazine./** Tratamiento de la esquizofrenia aguda con la sulforidazina. Revista de Neuropsiquiatria (Lima). 38(2):94-105, 1975.

The results of a therapeutic trial of sulphoridazine in the treatment of schizophrenia conducted on 20 acute or subacute patients are reported. The drug was administered 50mg i.m. every 4, 6 or 8 hours during the first 2 or 3 days, then 300mg per os until an effective dosage was found. Results indicate that 16 of the 20 patients experienced varying degrees of recovery from schizophrenic symptoms. According to the Overall and Gorham behavioral scales, the patients showed positive improvements on such symptoms as mental confusion, attitudes, hostility, and hallucinatory behavior. The effective dosage of sulphoridazine was found to range between

40mg and 300mg. Further controlled trials using other behavior scales are recommended. 13 references. (Journal abstract modified)

241277 Levenson, Alvin J. Dept. of Psychiatry, Baylor College of Medicine, Houston, TX **Intramuscularly administered fluphenazine HCl in acute/schizophrenia: a retrospective study.** Current Therapeutic Research. 19(3):320-327, 1976.

The clinical course of five acute schizophrenic inpatients, arbitrarily selected for treatment with a predetermined regimen of intramuscularly administered fluphenazine HCl (Prolixin HCl, nondepot), were retrospectively studied for speed and completeness of remission. The results of the review suggest this regimen to be a highly efficacious one, aiding in the production of a mean time to complete remission of psychotic signs and symptoms of 8.2days from inception of treatment. 33 references. (Author abstract)

241459 Stanford, John. Community Psychiatric Nursing Services, Powick Hospital, England **Schizophrenia: an end to relapses.** Nursing Times (London). 72(11):418-420, 1976.

A dramatic fall in the readmission rate of schizophrenics to Powick Hospital in England is attributed to the start of community psychiatric nursing by the hospital staff and the prescribing of long-acting phenothiazine injections, namely fluphenazine decanoate (Modecate). It is reported that, of 40 discharged patients, 30 are working full-time, two parttime, six are unemployed and two are over 65, as compared with a readmission rate for schizophrenics in the past of about 50%. A case study is presented to illustrate the success of this type of outpatient treatment. 2 references.

241760 Dick, Pierre; Remy, M.; Rey-Bellet, J. J. Clinique psychiatrique de l'Universite, Bel-Air, CH-1225 Chene-Bourg, Switzerland **/Comparison trial of two antipsychotic drugs: chlorpromazine and clozapine./** Essai de comparaison de deux antipsychotiques: la chlorpromazine et la clozapine. Therapeutische Umschau (Revue Therapeutique) (Bern). 32(8):497-500, 1975.

The results of a double-blind clinical trial comparing clozapine with chlorpromazine in 40 cases of chronic schizophrenia are reported. The therapeutic effectiveness of clozapine was shown to be at least equal to that of chlorpromazine. The observed tolerance was good. The observed side-effects of clozapine, such as sedation and slight extrapyramidal signs, suggest that this drug has a unique pharmacological action. 7 references. (Journal abstract modified)

241761 Woggon, Brigitte. Psychiatrische Universitatsklinik, Postfach 68, Lenggstrasse 31, CH-8029 Zurich 8, Switzerland **/Depot neuroleptics -- practical methods of long-term treatment and methodological problems of clinical trials./** Depotneuroleptica -- praktische Durchfuhrung der Langzeitbehandlung und methodische Schwiergkeiten bei der klinischen Prufung. Therapeutische Umschau (Revue Therapeutique) (Bern). 32(8):501-506, 1975.

Factors in the long-term treatment of schizophrenia with depot neuroleptics are discussed, including indications, advantages and disadvantages, beginning and duration of treatment, duration of effect, dosage and side-effects. Five depot neuroleptics are discussed: pipotiazine palmitate, fluphenazine decanoate, flupenthixol decanoate, fluspirilene and penfluridol. In addition, methodological problems of clinical trials with depot neuroleptics are described. 47 references. (Journal abstract modified)

241872 Domino, Edward F. Dept. of Pharmacology, University of Michigan, Ann Arbor, MI 48104 **The indole hallucinogen model: is it worth pursuing?** In: Suidlovsky, A., Predictability in psychopharmacology. New York, Raven Press, 1975. (p. 247-268).

Evidence which establishes the indole hallucinogen model as a useful method of obtaining new insight and developing new drugs of value in the treatment of schizophrenia is presented. Current biochemical theories and preclinical models of schizophrenia are considered. In this context, it is noted that of the many subtances which are known to be hallucinogenic, only the methylated indole alkylamines, such as dimethyltryptamine (DMT) and 5-methoxy-DMT, can be produced endogenously. Biosynthetic pathways for the formation of indole hallucinogens are delineated, and the possibility that some schizophrenic patients are "walking hallucinogen factories" is considered, particularly in terms of implications for new therapeutic approaches to schizophrenia. It is recommended that research efforts be directed toward the development of DMT models of schizophrenia in animals in the effort to find DMT antagonists as potential neuroleptic agents. 104 references.

241912 van Praag, H. M.; Korf, J. no address **/Biochemical research in schizophrenia: resulting in a new research strategy./** Biochemisch onderzoek van schizofrenie: resultaten van een nieuwe researchstrategie. Tijdschrift voor Psychiatrie (Meppel). 17(2):79-94, 1975.

It is contended that results of biological schizophrenia research have been unimpressive, and that the lack of proper research strategy has substantially contributed to this situation. It is suggested that neuroleptics can fill this gap by serving as a crystallization point for working hypotheses. The properties of neuroleptics are briefly discussed, and a research strategy is mapped. Results of a comparative study of chlorpromazine and oxypertine are reported. Chlorpromazine was selected because it is believed to reduce both dopaminergic and noradrenergic transmission, and oxypertine was selected because it is a more selective blocker of noradrenergic transmission. On the basis of this biochemical difference three hypotheses predicting clinical differences were formulated and tested. These hypotheses were generally confirmed. In view of this it seems likely that the biochemical action profile of neuroleptics is a more reliable indicator of their clinical action profile than their chemical structure. 25 references. (Journal abstract modified)

241936 Klerman, Gerald L. Dept. of Psychiatry, Harvard Medical School, Cambridge, MA **Pharmacotherapy of schizophrenia.** Annual Review of Medicine. 25:199-217, 1974.

The classes of compounds used in the pharmacotherapy of schizophrenia are reviewed and their therapeutic use is related to currently available information about modes of action of the compounds. The clinical disorder itself is described, with attention directed toward various symptoms: thinking and speech disturbances, catatonic motor behavior, paranoid ideation and behavior, schizophrenic hallucinations, delusional thinking, disturbances of affect and emotion, and disturbances of social behavior and interpersonal relations. Classes of compounds identified include phenothiazines, thioxanthenes, butyrophenones, Rauwolfias, benzoquinolines, and megavitamins. Therapeutic uses are outlined with regard to acute psychotic states, dosage recommendations, maintenance treatment, other therapies, and adverse effects. Pharmacological actions and the effects on the extrapyramidal nervous system and dopamine metabolism are also reviewed. Implica-

tions for future treatment of schizophrenia are considered. 40 references.

242503 Teutsch, H.; Boissl, K. W. D-8094 Gabersee, Bezirkskrankenhaus, Germany **/Experiences with a depot neuroleptic (Dapotum D)./** Erfahrungen mit dem Depotneuroleptikum Dapotum D. Medizinische Welt (Stuttgart). 25(48):2027-2032, 1974.

The use of Dapotum D, a depot neuroleptic, in a group of acute and chronic schizophrenics ranging in age from 18 to 80 years is reported. The positive treatment results obtained correspond with reports in the literature, and side-effects were below those generally reported. The recidivism rate is minimal. It is noted that triweekly injections have a less negative effect on the psychologically ill than daily oral injections, as the patient feels less dependent on family members and is more accepting of direct medical authority. At the same time, the therapy can be controlled with greater accuracy and with a lower suicide risk. A one year minimum treatment period is suggested for chronic schizophrenics. A low effective dosage of the drug promises reduced organ toxicity and fewer extrapyramidal effects, even over prolonged use. 56 references.

09 DRUG TRIALS IN AFFECTIVE DISORDERS

239002 Mindus, P.; Cronholm, B.; Levander, S. E. Dept. of Psychiatry, Karolinska Hospital, S-104 01 Stockholm 60, Sweden **Does piracetam counteract the ECT-induced memory dysfunctions in depressed patients?** Acta Psychiatrica Scandinavica (Kobenhavn). 51(5):319-326, 1975.

A double-blind, intraindividual crossover comparison of the effect of piracetam on retrograde memory impairment as measured by the KS memory test battery was performed in connection with second and third bielectroconvulsive therapy (Bi-ECT) in 18 inpatients diagnosed as suffering from depression. The seizure duration and the post-ECT electroencephalogram (EEG) patterns were examined visually and the post-ECT confusion time was measured. Piracetam was given orally in the dose of 4.8g/day for 3 days. No significant effects were obtained on memory scores, electrical stimulus duration, EEG pattern or post-FCT confusion time. It is suggested that the protective effect of piracetam shown in animal electroconvulsive stimulation (ECS) is due to a counteraction of the disturbing effect of hypoxia on memory functions. It is concluded that more information is needed as regards the pharmacokinetics and the mode of action of the drug. 21 references. (Author abstract)

239348 Hopkinson, G.; Kenny, F. Dept. of Psychiatry, Memorial University of Newfoundland, St. John's, Newfoundland, Canada **Treatment with reserpine of patients resistant to tricyclic antidepressants: a double-blind trial.** Psychiatria Clinica (Basel). 8(3):109-114, 1975.

The effects of reserpine administered simultaneously with tricyclic antidepressants to patients who previously failed to respond to tricyclic antidepressant therapy were assessed in a double-blind investigation of 14 patients. Eight Ss were administered 5mg of reserpine i.m.,and six were given 2ml of normal saline on two successive days. All patients continued on their current dosage of imipramine, trimipramine, or amitriptyline. The Hamilton Depressive Rating Scale was administered on the day before treatment began and was repeated on the fourth day. Findings indicate that the patients who received reserpine showed highly significant improvement. The mean fall in Hamilton scores for the placebo group was 6 points, and in the reserpine group it was 18.87. The therapeutic significance of the findings is discussed. 6 references. (Author abstract modified)

239615 Cocchi, Renato. Centri di Igiene Mentale della Provincia di Pesaro, Urbino, Italy **/Outpatient treatment with long-acting perphenazine (perphenazine enanthate): three cases./** Trattamento ambulatoriale con perfenazina ritardo (Trilafon enantato): 3 casi. Rassegna di Studi Psichiatrici (Siena). 64(5):789-798, 1975.

The treatment of three outpatients with perphenazine enanthate is described. All three patients exhibited symptoms of depression during treatment. Orphenadrine, in doses used with parkinsonian, neuroleptic induced symptoms, evidently does not have an adequate antidepressant effect. In one patient, lorazepam controlled mild symptoms. 1-Glutamine was administered to another patient and seemed to block the depression and hallucinations. Chlorimipramine also gave good results. It is concluded that perphenazine enanthate is an effective long-acting neuroleptic drug, but that it may cause secondary depression with concomitant suicidal tendencies. 27 references.

239728 Ebstein, Richard; Belmaker, Robert; Grunhaus, Leon; Rimon, Ranan. Jerusalem Mental Health Center-Ezrath Nashim, POB 140, Jerusalem, Israel **Lithium inhibition of adrenaline-stimulated adenylate cyclase in humans.** Nature (London). 259(5542):411-413, 1976.

The effects of therapeutic doses of lithium on plasma cyclic adenosine-3′,5′-monophosphate (cAMP) response to administration of adrenaline were investigated in a group of lithium treated and control subjects. Results indicate no mean increase in plasma cAMP levels after adrenaline injection in the lithium group, in contrast to the expected rise seen in control subjects. No effects of lithium were observed on basal adenylate cyclase activity; lithium appears to inhibit peripheral beta-adrenergic stimulation of the enzyme. The compatability of these results with the catecholamine hypothesis of affective disorders is considered. 21 references.

239820 Herridge, C. F. West Middlesex Hospital, Isleworth, Middlesex, England **A retrospective assessment of the long-term effects of dothiepin.** International Pharmacopsychiatry (Basel). 10(4):208-212, 1975.

A hospital based study of the treatment with dothiepin hydrochloride (Prothiaden) of 237 depressed patients, some for over 2 years, is reported. Of the initial 237 patients, 84 had to be withdrawn from the study, over one third of these because of nonattendance. Only 26 (11.8%) of all patients failed to respond and 23 (9.7%) had to be withdrawn because of side-effects, the most common being dry mouth (six patients) and drowsiness (four). The dosage required was between 75 and 225mg/day with 75% of patients receiving between 125 and 150mg/day. The majority of patients (75.2%) were well and off therapy by 9 months but a hard core of 30 patients (19.6%) required long-term treatment in excess of 2 years. It is concluded that dothiepin is a well tolerated, safe and effective antidepressant with a special place in the treatment of chronic depressive states in inadequate personalities. 5 references. (Author abstract)

239937 Quitkin, Frederic; Rifkin, Arthur; Klein, Donald F. Hillside Division, Long Island Jewish-Hillside Medical Center, PO Box 38, Glen Oaks, NY 11004 **Prophylaxis of affective disorders: current status of knowledge.** Archives of General Psychiatry. 33(3):337-341, 1976.

Evidence for prophylaxis of bipolar manic-depressive illness, unipolar depressive illness and schizoaffective illness is reviewed. For each disorder guidelines for prescribing prophylactic regimens are discussed. The literature review indicates that lithium carbonate is prophylactic for mania in bipolar patients. Studies are outlined that would clarify lithium carbonate's prophylactic effect for depression in unipolar and bipolar patient groups. Continuation therapy with antidepressants reduces incidences of recurrence in unipolar depressives. The only controlled study indicates that tricyclic antidepressants may have prophylactic effect in unipolar patients. This finding needs confirmation. Data are insufficient for conclusions on prophylactic treatment for schizoaffective disorders. 25 references. (Author abstract modified)

240032 Brasseur, R. Rue de Linthout 152, B-1040 Brussels, Belgium **/Double-blind trial of Diffucaps amitriptyline and ordinary amitriptyline in sleep disorders of depressive origin./** Comparaison en double insu entre l'amitriptyline Diffucaps et l'amitriptyline ordinaire dans les troubles du sommeil d'origine depressive. Acta Psychiatrica Belgica (Bruxelles). 75(2):182-189, 1975.

The effects of long-acting amitriptyline (Diffucaps) and ordinary amitriptyline were compared in a controlled drug trial. Ss were 35 patients suffering from sleep disorders resulting from depression. No other psychotropic substance was administered during the course of the trial. Diffucaps given in a dosage of 25mg at the evening meal were more active and better tolerated than a dosage of 40mg of ordinary amitriptyline given at bedtime. 2 references. (Journal sbtract modified)

240055 Bech, Per; Vendsborg, P. B.; Rafaelsen, O. J. Psychochemistry Institute, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark **Lithium maintenance treatment of manic-melancholic patients: its role in the daily routine.** Acta Psychiatrica Scandinavica (Kobenhavn). 53(1):70-81, 1976.

The effects of lithium prophylaxis were assessed in 76 manic-depressive patients who had accepted the necessity of a strict table regime. The evaluation was based on case history data and various rating scales. Results showed that in 24% of the patients, treatment was discontinued due to side-effects or insufficient effect. The suicide risk was not eliminated, and 29% of the patients were receiving additional antidepressive or antimanic treatment at the test day. However, 78% of the patients rated the relapse preventive lithium effect as moderate to excellent. Indirect evidence was obtained in support of a stabilizing effect of lithium on the emotional control in bipolar patients. The most frequent complaints during lithium treatment were tremor and increased thirst. 18 references. (Author abstract)

240216 Asberg, Marie. Dept. of Psychiatry, Karolinska Hospital, S-104 01 Stockholm 60, Sweden **Treatment of depression with tricyclic drugs -- pharmacokinetic and pharmacodynamic aspects.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 9(1):18-26, 1976.

A series of studies on the pharmacokinetic and pharmacodynamic properties of some tricyclic antidepressants is reviewed. During treatment with the same oral dose of these drugs, patients develop widely differing plasma levels. An association between side-effects and high plasma levels of nortriptyline is reported. The tricyclic antidepressants differ in their capacity to inhibit transmitter uptake into noradrenaline and serotonin neurons. These differential effects are also reflected in changes in the levels of the transmitter metabolites in cerebrospinal fluid (CSF). The CSF studies also support the hypotheses of a biochemical heterogeneity of the depressive syndrome. The levels of the serotonin metabolite, 5-hydroxyindoleacetic acid (5-HIAA) were bimodally distributed in CSF. In patients with a low level of 5-HIAA, there was a significant correlation between the CSF metabolite level and the severity of the depression, and these patients also appeared to be more suicide prone than those with higher 5-HIAA levels. These patients seemed to be less amenable to treatment with nortriptyline. 53 references. (Author abstract modified)

240217 Kragh-Sorensen, P.; Hansen, Chr. Eggert; Baastrup, P. Chr.; Hvidberg, E. F. Hvidovre Hospital, Neurology Dept., DK-2650 Hvidovre, Denmark **Relationship between antidepressant effect and plasma level of nortriptyline. Clinical studies.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 9(1):27-32, 1976.

Clinical studies of the relationship between antidepressant effect and plasma levels of nortriptyline (NT) are reviewed. Evidence is cited for the assumption that NT inhibits its own antidepressive effect at high but nontoxic plasma levels in patients suffering from endogenous depression. Based on three investigations, an optimal therapeutic plasma range for NT between 50 and 150ng NT/ml is recommended. 17 references. (Author abstract modified)

240707 Meyer, H.-H. Univ.-Nervenklinik, 665 Homburg-Saar, Germany **/Psychopharmacological therapy and prophylaxis of manic-depressive illnesses./** Die Psychopharmakotherapie und -prophylaxe der Manisch-depressiven Erkrankungen./ Medizinische Welt (Stuttgart). 26(25):1225-1229, 1975.

Psychopharmacological therapy of cyclothymia is outlined. A brief historical review of the therapeutic treatment of cyclothymia since 1935 is presented. Basic rules of psychopharmacological therapy are outlined, and tables describing the various antidepressant drugs available in Germany and their efficiency profiles are presented. Satisfactory results obtained with lithium salts as a prophylactic for endogenous depression are reported. Contraindications and concomitant symptoms such as muscular asthenia and vertigo are described. Aspects of suicide and manic-depressive illness are explained, and a strong control of the patient through his relatives or the doctor is recommended because of the strong suicidal tendency among manic-depressive individuals. 25 references.

240773 no author. no address **Tryptophan and depression.** British Medical Journal (London). No. 6004:242-243, 1976.

Research reported at a one day meeting held at the Royal College of Physicians to try to assess the usefulness of L-tryptophan in treating depression, either alone or in combination with other drugs, is summarized. It was found that while tryptophan availability seems important in controlling brain serotonin concentrations, the evidence as to whether there are changes in its availability in depressed patients is conflicting. It is concluded that more clinical studies on the use of L-tryptophan in depression are needed before a conclusion can be reached on its role, especially when combined with other antidepressant drugs. 19 references.

240839 Abdala, E. N. Castex 3293, Buenos Aires, Argentina **/Combination of tricyclic antidepressants and MAOI in depression./** Asociacion de antidepresivos triciclicos e IMAO en las depresiones. Acta Psiquiatrica y Psicologica de America Latina (Buenos Aires). 21(1):52-55, 1975.

Therapeutic effects and side-effects of combined treatment with tricyclic antidepressants and monoamine oxidase inhibitors (MAOI) were investigated in 122 depressive patients. All Ss reviewed both isocarboxazide and trimipramine three times a day. The following results are reported: 1) there were no serious side-effects; 2) the minor side-effects noted were no different from those observed with other tricyclics; 3) therapeutic doses were lower than those necessary when either drug is administered alone; 4) the speed of action was higher than in separate administration; 5) the overall percentage of improvement was higher than the percentage obtained for either drug separately; and 6) the lack of side-effects is attributed to the neuroleptic action of trimipramine. 6 references. (Journal abstract modified)

241762 Fleischhauer, J. Psychiatrische Universitatsklinik, Wilhelm-Klein-Strasse 27, CH-4025 Basel, Switzerland **/The psychopharmaceutical therapy of depression./** Zur Therapie der Depressionen mit Psychopharmaka. Therapeutische Umschau (Revue Therapeutique) (Bern). 32(8):507-514, 1975.

It is suggested that since most of the depressive patients are treated today as outpatients, some important questions must be clarified before treatment is started. The most important points are the suicide risk, the severity of the illness and the nosological and syndromatological form of the depressive syndrome. After the decision to treat the patient with antidepressants, the best way to start treatment is to begin with an antidepressant with central sedative effects in slowly increasing doses. If the desired clinical effect is achieved, the dosage can be decreased slowly. To prevent further depressive periods or periods of manic-depressive psychosis, lithium salts should be prescribed. The side-effects of antidepressants and lithium salts are discussed. The patient must be made aware of the alcohol potentiating effect of the antidepressants, and of the interference of drugs and alcohol on driving ability. 9 references. (Journal abstract modified)

241849 Suwana, Arun B. Department of Psychiatry, Mahidol University, Bangkok, Thailand **Remission of vitiligo and salt medication.** Journal of the Medical Association of Thailand (Bangkok). 58(6):337-338, 1975.

The case of a 57-year-old male Chinese patient who suffered depressive attacks and hypomania is discussed. He had developed white patches on the skin (vitiligo) over 20 years ago. To treat his mental condition, lithium was administered, but toxicity resulted and subsequently he was taken off the lithium. When his blood examination was found to be negative for lithium, the medication was started with 600mg/day. His mental and skin condition improved considerably. It is not known whether the vitiligo was psychosomatic in nature or the lithium salt had a pharmacological effect on skin disease. 3 references.

241875 Santos Moreira, Mario. Rua Rosario, 135, 3.0 andar, 20.000 Rio de Janeiro, Brazil **/The psychiatry of the female climacterium: neurotic or psychotic symptoms?/** Quadro psiquiatrico do climaterio feminino: sintomas neuroticos ou psicoticos? Revista Brasileira de Medicina (Rio de Janeiro). 32(12):774-777, 1975.

Psychological and biochemical aspects of the female climaterium are explained, emphasizing the effects of estrogen, plasma monoamine oxidase activity and serotonin in the general and sexual behavior of women at this time of life. The mental symptoms of this period are described as primarily psychotic as opposed to neurotic. It is suggested, therefore, that they be treated with phenothiazines rather than with drugs of the diazepine group. 12 references. (Journal abstract modified)

241937 Schildkraut, Joseph J. Neuropsychopharmacology Laboratory, Massachusetts Mental Health Center, Boston, MA **Biogenic amines and affective disorders.** Annual Review of Medicine. 25:333-348, 1974.

Recent studies of biogenic amines and affective disorders are reviewed, with emphasis on areas of research that appear most likely to yield biochemical criteria for classifying different types of affective disorders and predicting differential responses to various forms of treatment. Consideration is given to 3-methyl-4-hydroxyphenylglycol, homovanillic acid, 5-hydroxyindoleacetic acid, dopamine-beta-hydroxylase activity, catechol-O-methyl transferase activity, and monamine oxidase activity. The findings suggest important clues to the different pathophysiological substrates underlying the biological heterogeneity of affective disorders. They also appear to support the possibility that different subgroups of patients with depressive disorders may exhibit different specific abnormalities in the metabolism of norepinephrine or other biogenic amines. The findings are compatible with the suggestion that, in patients with affective disorders, certain changes in biogenic amine metabolism may occur in association with changes in affective state, whereas other abnormalities in monoamine metabolism may represent enduring consitutional factors. 119 references.

242248 Singh, A. N.; Saxena, B.; Gent, M.; Nelson, H. L. P.O. Box 585, Hamilton, Ontario, Canada **Maprotiline (Ludiomil, CIBA 34,276-BA) and imipramine in depressed outpatients: a double-blind clinical study.** Current Therapeutic Research. 19(4):451-462, 1976.

A double-blind clinical trial of 6 weeks duration with 30 depressed patients was conducted to compare the antidepressant activity of maprotiline (Ludiomil) to that of imipramine. Several standard rating scales were used to assess depression, as well as specific psychiatric, neurophysiological, physical and laboratory examinations. The results show that maprotiline was an effective and well tolerated antidepressant drug, its overall therapeutic activity being statistically superior and qualitatively different from the reference drug. 7 references. (Author abstract modified)

242249 Lehmann, H. E.; Pecknold, J. C.; Ban, T. A.; Orbach, Leora. Div. of Psychopharmacology, Dept. of Psychiatry, McGill Univ., Montreal, Quebec, Canada **A double-blind comparative clinical trial with maprotiline (Ludiomil) and imipramine in newly-admitted depressed patients.** Current Therapeutic Research. 19(4):463-468, 1976.

A double-blind clinical trial was conducted to compare the therapeutic and adverse effects of maprotiline and imipramine. On the basis of observations of 40 depressed psychiatric ambulatory patients evaluated by the Hamilton Psychiatric Rating Scale, the Brief Psychiatric Rating Scale, the Zung Self-Rating Depression Scale, and the Clinical Global Impressions Scale, it is suggested that maprotiline, a tetracyclic substance, in a dosage of 50mg to 150mg per day, is equal or superior in its therapeutic efficacy to imipramine, a standard tricyclic antidepressant drug. The composition of the patient population differed from that studied in an earlier maprotiline/amitriptyline trial in that there were only two bipolar depressed patients in the imipramine and one bipolar patient in the maprotiline group. All three improved, and none developed a manic reaction. 1 reference. (Author abstract)

242251 Sathananthan, Gregory; Mir, Pervez; Minn, Fredrick L.; Gershon, Samuel. Neuropsychopharmacology Research Unit, New York Univ. Medical Ctr., 550 First Ave., New York, NY 10016 **Antidepressant predictability: cartazolate.** Current Therapeutic Research. 19(4):475-478, 1976.

Ten inpatients manifesting moderate to severe symptoms of psychotic depression were treated openly with cartazolate, a potent cyclic adenosine monophosphate phosphodiesterase inhibitor. In a previous study it had been reported that this compound had nonsedative anxiolytic properties. A major question for this clinical trial was to explore the clinical predictability based on several established preclinical tests of antidepressant activity. At the end of the study, four patients improved. The nonresponders also did not respond to imipramine. None of the patients reported any side-effects. The combination of both antidepressant and anxiolytic properties in this compound warrants further investigation. 2 references. (Author abstract)

10 DRUG TRIALS IN NEUROSES

238981 Weissman, Myrna M.; Lieb, Julian; Prusoff, Brigitte; Bothwell, Sallye. Connecticut Mental Health Ctr., 904 Howard Ave., Suite 5, New Haven, CT 06519 **A double-blind trial of maprotiline (Ludiomil) and amitriptyline in depressed outpatients.** Acta Psychiatrica Scandinavica (Kobenhavn). 52(4):225-236, 1975.

The results of a double-blind trial of a tetracyclic antidepressant, maprotiline (Ludiomil) and a conventional tricyclic, amitriptyline (Elavil), in 67 ambulatory depressives are reported. Hamilton's Rating Scale for Depression was the main outcome criterion. No statistically significant differences were found between the drugs in onset of action, efficacy, side-effects or predictors of response. Patients on either drug showed a significant reduction in symptoms after 1 week of treatment and at the end of the trial. Both drugs were tolerated well. A review of previous double-blind comparisons of maprotiline and tricyclic antidepressants is also included, revealing similar results. The main outcome criterion in all these studies was manifest psychopathology assessed on the Hamilton Rating Scale for Depression by the treating physician. The absence of additional types of outcome criteria or assessment techniques, which may have detected differences in motor activity or drive as originally postulated, may have obscured results which were expected to be subtle. 21 references. (Author abstract modified)

239022 Siciliani, Orazio; Schiavon, Michele; Tansella, Michele. Psychiatric Univ. Clinic of Verona, Policlinico di Borgo Roma, I-37100 Verona, Italy **Anxiety and EEG alpha activity in neurotic patients.** Acta Psychiatrica Scandinavica (Kobenhavn). 52(2):116-131, 1975.

The literature on electroencephalogram (EEG) alpha activity in different psychological states is reviewed and 20 male neurotic inpatients suffering from chronic moderate anxiety were assessed with respect to anxiety level and EEG alpha activity (frequency and percent time) and fast activity. No significant EEG asymmetry was found. The average alpha percent time was very low, most of the patients being low alpha subjects. Anxiety and alpha index were significantly correlated. The patients were then treated with either 80mg per day of temazepam or placebo for 2 weeks (double-blind). Significant effects were detected in the anxiety state, the drug group showing more improvement, but not in the EEG profile. The measures were expressed at this stage as change scores from the pretreatment values, and correlations between them were computed. The only correlation of significance was a negative correlation between anxiety level and alpha index found after a week in the drug group. 66 references. (Author abstract)

239818 Trick, K. L. K. St. Crispin's Hospital, Northampton, England **Double-blind comparison of maprotiline with amitriptyline in the treatment of depressive illness.** International Pharmacopsychiatry (Basel). 10(4):193-198, 1975.

Thirty patients closely matched for age, sex and duration of illness were treated with either amitriptyline or maprotiline in a double-blind, between patient trial. Within the limits of the small number of patients in the trial, maprotiline produced a significantly quicker improvement during the first 2 weeks as judged by the scores on the Hamilton Rating Scale. Maprotiline showed better tolerability than amitriptyline overall, especially as far as trial dropout rates were concerned. 3 references. (Author abstract)

239938 Ravaris, C. Lewis; Nies, Alexander; Robinson, Donald S.; Ives, John O.; Lamborn, Kathleen R.; Korson, Lorraine. Dept. of Psychiatry, Univ. of Vermont College of Medicine, Burlington, VT 05401 **A multiple-dose, controlled study of phenelzine in depression-anxiety states.** Archives of General Psychiatry. 33(3):347-350, 1976.

The dose/response relationship of phenelzine in depression/anxiety states was studied. In a double-blind, controlled experiment, 62 outpatients with symptoms of depression with anxiety were selected for treatment with phenelzine sulfate, 60mg daily, phenelzine sulfate, 30mg daily, or placebo for 6 weeks. Forty-nine patients (79%) completed the experiment. Phenelzine sulfate, 60mg daily, was significantly more effective than placebo in relieving symptoms of both depression and anxiety. Phenelzine sulfate, 60mg daily, resulted in a median inhibition of platelet monoamine oxidase that exceeded 80%. The results confirm a previous study that found phenelzine to be effective in the treatment of outpatients with depressive anxiety states. Drug dosage is an important variable influencing clinical outcome in this patient group. 21 references. (Author abstract)

240694 no author. no address **Beta-blockers in anxiety and stress.** British Medical Journal (London). No. 6007:415, 1976.

The use of beta-adrenergic blocking agents, such as propranolol or oxprenolol, in combination with centrally acting sedatives for the treatment of anxious patients was suggested at a recent symposium of medical scientists and clinicans. It is recommended that propranolol be administered in doses of about 60 to 240mg daily. A use of beta-blockers for attenuation of the physiological consequences of normal mental stress is also suggested. The value of beta-blockers in other conditions, such as mania, schizophrenia, opiate and other drug withdrawal, alcoholism, essential tremor and Parkinsonian tremor is questioned. The use of these agents for amphetamine withdrawal is suggested as a possible exception. 5 references.

241275 Itil, Turan M.; Akpinar, Sevket; Fink, Max; Polvin, Necmettin; Hugue, Mohammed; Sungurbey, Kemal. HZI Neuropsychiatric Foundation, Istanbul, Turkey **Controlled clinical and quantitative EEG studies of triflubazam (ORF 8063) in patients with anxiety syndrome.** Current Therapeutic Research. 19(3):307-315, 1976.

The anxiolytic activity and duration of activity of triflubazam (ORF-8063) was examined in male and female Ss with anxiety reactions. Daily doses of 30mg elicited minimal anxiolytic activity, no greater than that seen in placebo treated patients. Electroencephalographic (EEG) records showed no ac-

tivity related to triflubazam at 1 and 3 hours after a single oral dose, but the typical anxiolytic cortical EEG profiles were seen after 1 and 3 weeks. This finding contrasts with the rapid onset of EEG changes after single doses of such anxiolytics as diazepam and chlorazepate which elicit evidence of central nervous system activity within 30 minutes of ingestion. The lack of clinical success with triflubazam in this study is attributed to the low initial dosage and slow buildup. It is suggested that trials using higher intial doses should be considered particularly since there was no evidence of toxicity in this study. 10 references.

241278 Fabre, Louis F., Jr.; Harris, Robert T. Fabre Clinic, Houston, TX **Pilot open-label study of lenperone (AHR 2277), a butyrophenone, in anxiety.** Current Therapeutic Research. 19(3):328-336, 191976.

Twenty outpatients with anxiety nuerosis of sufficient intensity to score at least 20 on the Hamilton Anxiety Scale, were treated with lenperone (AHR-2277) in an uncontrolled study. Anxiety symptoms were considerably ameliorated at 7 days, and this improvement persisted throughout the 21 day study period. The optimal dose for clinical improvement was 10mg/day given in divided doses. Eight patients dropped out during the study and were replaced so that 20 completed. Six dropped midway for reasons unrelated to the study and two for side-effects of drowsiness and nasal congestion. All other routine laboratory examinations were unaltered by lenperone. 4 references. (Author abstract)

241427 Dasberg, H. "Esrath Nashim" Psychiatric Hospital, Hebrew University, Hadassah Medical School, P.O. Box 140, Jerusalem, Israel **Oral diazepam in hospitalized anxiety patients (with observations on concentration-effect-relationships).** Pharmakopsychatrie Neuro-Psychopharmakologie (Stuttgart). 8(4):162-169, 1975.

The anxiolytic efficacy of oral diazepam, 30mg daily, was investigated in newly admitted psychoneurotic patients who were suffering from anxiety syndromes. A double-blind crossover design against placebo was used. Ratings were performed weekly using the Hamilton scale for anxiety and other scales. Diazepam was significantly more effective than placebo for treating the global anxiety syndrome, as objectively and subjectively rated. The symptoms most sensitive to its action are anxious mood, psychic tension, behavioral unrest, insomnia and respiratory complaints; side-effects were few. Using Spearman rank correlation coefficients a significant concentration/effect/relationship was found for diazepam and desmethyldiazepam products. 28 references. (Author abstract)

241758 Lader, M. H. Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, England **/Anxiolytic medications./** Les medicaments anxiolytiques. Therapeutische Umschau (Revue Therapeutique) (Bern). 32(8):478-485, 1975.

It is suggested that anxiety is a common complaint which presents itself in many ways, and that recognition of its underlying causes is not always possible. When drugs are used, a finite course of treatment should be envisaged and the case should be reviewed if drug treatment drags on. Among the available anxiolytic drugs, the benzodiazepines have supplanted the barbiturates. A useful combination is that of a benzodiazepine and a beta-adrenoceptor blocking agent. In patients with histories of dependence on psychotropic agents including alcohol, major tranquilizers in small doses should be tried first. If depression is present as well as anxiety, a tricyclic antidepressant with sedative properties such as amitriptyline is the treatment of choice. 22 references. (Journal abstract modified)

241759 Al-Shaltchi, Beatrice; Poldinger, Walter Felix-Platter-Spital, Burgfelderstrasse 101, CH-4000 Basel, Switzerland **/Anxiolytic pharmacotherapy in general practice./** Anxiolytische Pharmakotherapie in der Praxis. Therapeutische Umschau (Revue Therapeutique) (Bern). 32(8):486-496, 1975.

It is suggested that since diagnosis is a prerequisite for any treatment, anxiety syndromes must be understood from a phenomenological standpoint. In this connection, the problem of the differentiation of anxiety from fear in nonmedical circumstances is discussed. Anxiety being a cardinal symptom of various illnesses, the significance of different forms of depression and their relationship to the danger of suicide is discussed. Since the pathogenesis of the anxiety syndrome is of great importance in determining therapy, attention must be given to the differences between "pure" anxiety, "pangs of conscience", neurotic anxiety, psychotic anxiety and existential anxiety. Various possibilities for the psychopharmaceutical treatment of anxiety syndromes are examined. 74 references. (Journal abstract modified)

242250 Gomez-Lozano, Pedro. Bogota, Colombia **Intravenous lorazepam in the acute anxiety crisis: a preliminary report on 60 cases.** Current Therapeutic Research. 19(4):469-474, 1976.

After the preliminary successful use of injectable lorazepam in calming 20 patients who presented with acute anxiety crises, a formal study of 40 other such patients was conducted. All 40 were seen either in a hospital emergency room or on an emergency outpatient basis in private practice. Treatment consisted of an initial intravenous injection of lorazepam (3mg) followed, if necessary, by up to three further injections within a 24 hour period. The result was usually dramatic: complete abolition of all symptoms within 5 to 30 minutes in 38 patients (95%), with only 3 requiring more than a single injection to maintain such improvement. The major effect was relaxant and sedative; 24 patients slept following the injections, although 22 of the 24 could be easily aroused. Of the other 16 patients, 14 remained awake but relaxed; only 2 remained tense and were regarded as failures. No significant side-effects or changes in vital signs were noted. The results support and extend those reported by another investigator in a recent controlled, double-blind (but otherwise similarly conducted) trial. 8 references. (Author abstract)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

238866 Worz, R.; Baar, H.; Draf, W.; Garcia, J; Gerbershagen, U.; Gross, D.; Magin, F.; Rieble, R.; Ritter, K.; Scheifele, J.; Scholl, W. Kirnerstrasse 1, 8870 Gunzburg, Germany **/On the multifactorial treatment of chronic headaches./** Zur Mehrfaktorenbehandlung bei Dauerkopfschmerzen. Nervenarzt (Berlin). 46(11):640-647, 1975.

The multifactorial treatment of patients with previously therapy resistant headaches is discussed. A report on the treatment of 60 women, suffering from chronic headaches for at least one year is presented. Through the therapeutic concept of coordinated multifactorial treatment, 10 patients were cured, 42 showed improvment, and 6 showed no improvement. The most important elements of this treatment are the withdrawal of analgesics, the use of local anesthesia where necessary, and psychotherapeutic measures. Thymoleptics and other psychopharmaceuticals were used only when necessary, and in small doses. The continued use and increased dosage of mixed analgesic preparations is absolutely contraindicated in such cases. 23 references.

238982 van Hemert, J. C. J. Dept. of Neurology, Maria Stichting, Heythuizenweg 1, Haarlem, The Netherlands **Pipamperone (Dipiperon, R 3 345) in troublesome mental retardates: a double-blind placebo controlled cross-over study with long-term follow-up.** Acta Psychiatrica Scandinavica (Kobenhavn). 52(4):237-245, 1975.

A 6 week double-blind crossover study comparing pipamperone with placebo was conducted in 20 female mental retardates with behavioral disorders. Ss ranged between 22 and 42 years of age. After a 2 week washout period, patients were randomly allocated to either pipamperone or placebo treatment. The initial dosage of pipamperone was 40mg b.i.d.,which was gradually increased to 80mg t.i.d. within 5 days. Patients were assessed using a 10 item rating scale before and after each week of treatment. For 6 of the 10 items, patients showed a better response during the pipamperone than during the placebo period. When pretrial scores were compared with those at the end of the trial, seven items had significantly improved with pipamperone. It is noted that the nursing staff also considered the patients more alert and amenable during pipamperone treatment. 9 references. (Author abstract modified)

238988 Altamura, Alfredo Carlo. Dept. of Clinical Psychiatry, University of Milan - Polyclinic, Via F. Sforza 35, 20122 Milan, Italy **Therapeutic attempts with lithium in young drug addicts.** Acta Psychiatrica Scandinavica (Kobenhavn). 52(5):312-319, 1975.

To test the hypothesis that drug addiction may be due to "masked depression", lithium was administered to 20 opiate addicts. Only nine patients took the lithium carbonate tablets for more than a few weeks; during this period they seemed to abstain from taking opiates. After 1 year, all the patients were off lithium and most of them again took opiates. Due to lack of cooperation on the part of the patients, the observations can neither confirm nor refute the hypothesis. The study shows that psychological and social environmental factors make trials on drug treatment of opiate addicts almost impossible to carry out. 20 references. (Author abstract)

239014 Riding, Joyce; Munro, Alistair. Dept. of Psychiatry, University of Liverpool, 6 Abercromby Square, Liverpool L69 3BX, England **Pimozide in the treatment of monosymptomatic hypochondriacal psychosis.** Acta Psychiatrica Scandinavica (Kobenhavn). 52(1):23-30, 1975.

The efficacy of pimozide in the treatment of monosymptomatic hypochondriacal psychosis, a disorder with a traditionally poor prognosis, was assessed in six cases. Results indicate that three patients responded favorably, one showed partial improvement, one showed marked improvement despite a possibility of early cerebral arteriopathy, and one showed no improvement. The one patient who showed no improvement was suspected all along of having a personality disorder rather than a psychotic illness, and this was subsequently confirmed. It is suggested that pimozide may be an effective treatment for monosymptomatic hypochondriacal psychoses whatever their etiology, may differentiate rapidly between cases of monosymptomatic hypochondriacal psychoses and dysmorphophobias due to neurotically determined factors. 8 references. (Author abstract)

239074 Share, Jack B. Psychology Dept., California State University, Northridge, CA 91324 **Review of drug treatment for Down's syndrome persons.** American Journal of Mental Deficiency. 80(4):388-393, 1976.

A review of drug treatment for Down's syndrome individuals is presented. Drugs used to modify behavior, as well as drugs used with the goal of affecting cognitive processes, are discussed. Some observations are offered as to the effectiveness of past and current drugs on Down's syndrome, and some methodological problems relating to drug studies are presented. It is concluded that there have not been any drugs that have demonstrated remarkable improvement in the status of Down's syndrome individuals that have been widely accepted as effective. 32 references. (Author abstract)

239269 Setyonegoro, R. Kusumanto; Dipojono, Bonokamsi. no address **Treatment of unselected Indonesian psychotic patients with Dogmatil (Delagrange).** Indonesian Psychiatric Quarterly (Djakarta). 8(2):1-10, 1975.

An open clinical trial of Dogmatil treatment for 102 unselected psychotic Indonesian patients is reported. Subjects were all psychotic patients admitted to six psychiatric clinics and seen by 16 military and civilian psychiatrists between September 1, 1973, and May 31, 1974, excluding those diagnosed as having chronic brain syndrome. They were treated with Dogmatil (sulpiride) for 42 days, and were tested using the Brief Psychiatric Rating Scale (BPRS) of Overall and Gorham. Results indicate that 78 of the patients showed a very good or good improvement. It is concluded that Dogmatil is a valuable antipsychotic drug. The often dramatic improvement recorded within a very short period (10 to 14 days) is cited as proof of the powerful neuroleptic capacities of the drug, especially in its injectable form. Side-effects were mild or minimal. It is suggested that further studies be conducted to yield data regarding Dogmatil treatment in selected cases. 9 references.

239346 Abe, Kazuhiko. Dept. of Psychiatry, Osaka City University Medical School, Abenoku, Osaka, Japan **Sulpiride in school phobia.** Psychiatria Clinica (Basel). 8(3):95-98, 1975.

The use of sulpiride in the treatment of school phobia children was evaluated in 21 children suffering from school phobia and depressive symptoms and who had been treated by nonpharmacological measures. Findings indicate that 13 returned to school within a few days, and depressive symptoms eventually disappeared. The home behavior of three Ss returned to premorbid status, but school refusal persisted. In the remaining five cases no improvement was observed. In comparison to previous studies with imipramine and benzodiazepines, the response to sulpiride in school phobic children was rapid and remarkable. 7 references. (Author abstract)

239641 Conforto, C.; Risso, A. M.; Solaro, F. Istituto di Psichiatrica, Universita di Genova, Genoa, Italy /**Reflections on psychiatric assistance in an outpatient geriatric center: the use of psychotropic drugs.**/ Considerazioni sull'assistenza psichiatrica in un centro geriatrico ambulatoriale: l'impiego degli psicofarmaci. Giornale di Gerontologia (Firenze). 23(8):696-704, 1975.

The use of psychotropic drugs in an outpatient geriatric center is discussed. Tricyclic antidepressants have been widely used in syndromes with symptoms of depression. The doses initially prescribed are low (10-20mg/day) and are gradually increased up to 100mg/day. Monoamine oxidase inhibitors can be used with geriatric patients, but possible toxic side-effects should be carefully considered. Phenothiazines seem to be the most useful of the neuroleptic drugs. However, all the neuroleptics cause a number of side-effects, including extrapyramidal disturbances, arterial hypotension, and disturbances in liver function. Thioridazine seems to be the

most manageable and least apt to cause side-effects. The benzodiazepines are rarely used in geriatric medicine due to paradoxical reactions. The use of barbituates is greatly contraindicated with geriatric patients and those with suspected organic brain syndrome. The most manageable nonbarbituate hypnotic drug seems to be methaqualone. 28 references.

239700 Borromei, A. Clinica per le Malattie Nervose e Mentali, Universita di Bologna, Italy **/Some therapeutic uses of GABA in neurology./** Alcuni impieghi terapeutici del GABA in neurologia. Rivista di Patologia Nervosa e Mentale (Firenze). 95(4):300-322, 1974.

At the Symposium on Central Nervous System Neurotransmitters, held in Rome, December 1973, therapeutic uses of gamma-aminobutyric acid (GABA) in neurology were discussed, based on clinical experiments. In particular, clinical results were reported with respect to 122 comatose patients following severe cranio-cerebral trauma. They were compared with those of a control group of 100 equivalent patients treated with classical resuscitation procedures; a decrease in overall mortality from 38 to 24.5% was found with the GABA treated Ss. This difference was even more significant when only deaths occurring within 90 days of the beginning of the coma were taken into account. The most probable hypotheses for explaining the anticoma effects of GABA were discussed. Other possible clinical uses of GABA in neuropsychiatry and general medicine range from infantile mental deficiency to arterial hypertension, thrombosis, brain hemorrhage, Parkinson's disease, and epileptic syndromes. 85 references. (Journal abstract modified)

239824 Hanlon, Thomas E.; McCabe, O. Lee; Savage, Charles; Kurland, Albert A. Maryland Psychiatric Research Center, Box 3235, Baltimore, MD 21228 **A controlled comparison of cyclazocine and naloxone treatment of the paroled narcotic addict.** International Pharmacopsychiatry (Basel). 10(4):240-250, 1975.

A controlled, double-blind study of the comparative effectiveness of the narcotic antagonists cyclazocine and naloxone was undertaken in a metropolitan narcotic clinic offering an abstinence program involving urine monitoring and ancillary counseling services. Seventy male addict parolees were randomly assigned to 6 month treatment with either cyclazocine, 4mg administered on a daily basis, or naloxone, 500-2000mg administered on a locally developed and researched contingent basis, i.e.,whenever there was indication of narcotic drug use (daily and contingent placebos were utilized to preserve the double-blind). Criteria of treatment effectiveness included narcotic drug usage, clinic attendance, length of participation in the program, disposition at 6 months, and incidence of side-effects. The two subsamples of 35 individuals were similar with respect to relevant demographic characteristics. Examination of comparative effects revealed little to no significant differences between the two groups in terms of measures of program adherence, treatment outcome, and personal and social adjustment. Side-effects were more prevalent among cyclazocine patients. Typically, these included moderately severe somatic effects and perceptual and cognitive disturbances. 10 references. (Author abstract)

239932 Arnold, L. Eugene; Huestis, Robert D.; Smeltzer, Donald J.; Scheib, James; Wemmer, Douglas; Colner, Gary. Dept. of Psychiatry, Ohio State Univ., College of Medicine, 473 W. 12th Ave., Columbus, OH 43210 **Levoamphetamine vs dextroamphetamine in minimal brain dysfunction: replication, time response, and differential effect by diagnostic group and family rating.** Archives of General Psychiatry. 33(3):292-301, 1976.

Double-blind crossover randomized Latin square comparison of placebo, dextroamphetamine, and levoamphetamine in 31 consecutively diagnosed children with minimal brain dysfunction (MBD) replicated a smaller nonrandom study. Both isomers showed significantly more benefit than placebo but were not significantly different from each other. Dextroamphetamine showed a nonsignificant trend of superiority over levoamphetamine. Of 25 subjects who responded well to drugs, 3 responded only to levoamphetamine, 5 only to dextroamphetamine, and 17 to both. This study seems to confirm the efficacy of levoamphetamine in MBD. An unsocialized aggressive subgroup showed a nonsignificant trend for levoamphetamine superiority, in contrast to the hyperkinetic and overanxious subgroups. Those who responded best to levoamphetamine tended (not significantly) to be from poorer functioning families. Parents' ratings, but not teachers' or psychiatrists' ratings showed significant placebo effect. 19 references. (Author abstract)

239939 Goldstein, Avram. Addiction Research Foundation, 701 Welch Rd., Palo Alto, CA 94304 **Heroin addiction: sequential treatment employing pharmacologic supports.** Archives of General Psychiatry. 33(3):353-358, 1976.

A system of treatment for heroin addiction is proposed under the acronym STEPS (sequential treatment employing pharmacological supports). Small steps characterized by decreasing narcotic induced euphoria and increasing social rehabilitation are expected eventually to bring the addict to an abstinent and well functioning state. The dichotomous assessment of success or failure is rejected in favor of the expectation of partial and temporary improvements, as with any chronic relapsing disease. 39 references. (Author abstract modified)

239941 Meyer, Roger E.; Mirin, Steven M.; Altman, Jack L.; McNamee, H. Brian. Alcohol and Drug Abuse Research Center, McLean Hospital, 115 Mill St., Belmont, MA 02178 **A behavioral paradigm for the evaluation of narcotic antagonists.** Archives of General Psychiatry. 33(3):371-377, 1976.

An experimental paradigm for the behavioral evaluation of narcotic antagonists was developed. The study specifically examined the heroin seeking behavior of hard-core narcotic addicts on a research ward under blocked and unblocked conditions. A long-term followup program in the community, with aftercare services, was utilized to determine the relationship between behavior observed on the research ward and behavior that occurred in the community. While preliminary 1 month followup data offered some cause for an optimistic view of narcotic antagonist treatment, behavioral data observed on the research ward raised serious doubts about the possibility of extinguishing heroin self-administration with antagonists. The behavioral data were not consistent with laboratory descriptions of extinction. Rather, the data suggest that narcotic antagonist programs should emphasize the development of contingencies for the reinforcement of narcotic antagonist self-administration to ensure an opiate free state, instead of focusing on an extinction approach. 29 references. (Author abstract modified)

240033 Van Laere, E.; De Mol, J. Service de Neurochirurgie, Universite Libre de Bruxelles, Rue Heger Bordet 1, B-1000 Brussels, Belgium **/Trial of a new therapeutic agent, Pervincamine, in the postconcussion syndrome of cranial traumas: application of a double-blind control and sequential analysis./**

Essai d'un nouvel agent therapeutique, la Pervincamine, dans le syndrome postcommotionnel des traumatises craniens: application d'une methode de controle a double anonymat et de l'analyse sequentielle. Acta Psychiatrica Belgica (Bruxelles). 75(2):190-207, 1975.

The effects of vincamine (Pervincamine) on the postconcussion syndrome were examined in a double-blind study of 30 patients with cranial trauma who were examined at least 6 months following their accident. Patients were followed at regular 3 week intervals. They were interviewed and were administered Zazzo's test and the Rey 15 word test. An electroencephalogram was performed at the beginning and end of the study. Statistical analysis of the evolution of symptoms and the results obtained by psychological testing revealed the positive action of Pervincamine on the postconcussion syndrome and on mental as well as motor functioning in general. Side-effects were negligible. 28 references. (Journal abstract modified)

240166 Brochier, F. Foundation de Rothschild, 76, rue Picpus, 75012 Paris, France /**The quality of intellectual life in the elderly: double-blind study of Hydrosarpan-711 in 80 subjects.**/ La qualite de la vie intellectuelle des personnes agees: etude en double aveugle d'Hydrosarpan 711 portant sur 80 sujets. Revue de Gerontologie d'Expression Francaise (Paris). No. 5:58-61, 1975.

A double-blind study of the effects of Hydrosarpan-711 on the quality of intellectual life in the elderly is reported. Tolerance to the drug over 6 months was excellent. Improvement was found on all the tests used, but mainly on those involving general intelligence. Only the performances obtained during the "series of letters" test were worse for the drug than for the placebo. In addition, the treatment gave the elderly patient a "sense of well-being" due to the disappearance of many subjective disturbances such as dizziness, buzzing in the ears, feelings of light headedness.

240219 Schilkrut, R.; Ruther, E.; Ackenheil, M; Eben, E.; Hippius, H. Dept. of Psychiatry, Univ. of Chile, Santiago de Chile, Chile **Clinical and biochemical parameters during neuroleptic treatment: II. Antipsychotic effect of haloperidol in patients with chronic organic brain damage.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 9(1):37-42, 1976.

The time course of psychopathological symptoms, of extrapyramidal side-effects, and of changes in cerebrospinal fluid (CSF) concentrations of homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA) were simultaneously studied during haloperidol treatment of 14 psychotic patients with chronic organic brain damage. After 15 days of treatment, significant antipsychotic effect was found, while Parkinsonism scores in clinical and experimental tests increased only slightly. CSF concentration of HVA increased significantly by 150% compared to the baseline value, and 5-HIAA remained unchanged. No correlation was found between the clinical and biochemical variables studied. The comparison of these results with those obtained in patients without brain damage suggests that different psychopathological and extrapyramidal responses to neuroleptics are not strictly associated with specific HVA changes in CSF. 21 references. (Author abstract)

240260 Baust, W. Neurologische Universitatsklinik, Moorenstrasse 5, 4 Dusseldorf, Germany /**Sleep attacks.**/ Schlafanfalle. Medizinische Welt (Stuttgart). 26(12):563-566, 1975.

The differential diagnosis of sleep attacks and narcolepsy is discussed, and it is suggested that sleep attacks show the same general characteristics as normal sleep, but that electroencephalography reveals disturbances in rapid eye movement (REM) sleep and nonREM sleep in most cases. Many cases of sleep attacks are complicated by cataplexy or hypnagogic hallucinations. Possibilities for the psychopharmacological symptom specific treatment of sleep disturbances are discussed, and nacolepsy caused by the Pickwick syndrome, a disturbance in breathing regulation leading to hypoxia, is examined. 11 references.

240423 Hafner, R. J.; Crisp, A. H.; McNeilly, A. S. Academic Dept. of Psychiatry, St. George's Hospital, London SW17, England **Prolactin and gonadotrophin activity in females treated for anorexia nervosa.** Postgraduate Medical Journal (Oxford). 52(604):76-79, 1976.

The nature of the hypothalamic dysfunction underlying anorexia nervosa was investigated by assaying the activity of prolactin, luteinizing hormone, and follicle stimulating hormone in 13 female patients who were being treated with phenothiazines. Results indicate that premorbid obesity was significantly associated with higher prolactin levels and higher phenothiazine dosage during the weight gain recovery period and more weakly associated with a failure to resume gonadotrophic and menstrual activity. The patients could be differentiated into two distinct groups, based on the pattern of hormonal changes, as correlated with premorbid tendencies toward obesity. Possible explanations for these differences during the recovery period are advanced, with emphasis on the effects of arousal and emotional distress on hypothalamic function and gonadotrophic activity. 9 references.

240538 Rie, Herbert E.; Rie, Ellen D.; Stewart, Sandra; Ambuel, J. Philip. Dept. of Pediatrics, Ohio State Univ., Children's Hospital, Columbus, OH 43205 **Effects of methylphenidate on underachieving children.** Journal of Consulting and Clinical Psychology. 44(2):250-260, 1976.

The effects of methylphenidate hydrochloride (Ritalin) on the achievement and behavior of primary grade children were studied, and the reactions of 28 children to active drug and placebo were compared. In a double-blind counterbalanced design, each treatment condition was maintained for 12 weeks. Using multiple medical and psychological measures, as well as a full length, standardized achievement test and behavior ratings, the typical suppressive behavioral effects were observed. No substantial drug effects on achievement were found, and pretreatment evaluations failed to support the common assumption of concomitance among hyperactivity, minimal brain dysfunction, and learning disorder. Reduced responsivity on active drug treatment was observed clinically. It is urged that effects of Ritalin on specific functions be considered rather than global effects without specifications, and it is concluded that Ritalin should not be used to "treat" learning disorders. 32 references.

240657 Gilbert, Jean-Claude; Willer, Jean-Claude; Bernheim-Chaltelain, Chantal; Ecoffet, Michel; Jaillon, Patrice. Hopital Saint Antione, Paris, France **Narcolepsy: REM sleep suppression by L-dopa.** New England Journal of Medicine. 294(15):849, 1976.

The possibility of dysregulation of central monoamines was investigated in a narcoleptic patient who volunteered for two 48 hour periods of study. Polygraphic recordings showed that total sleep time was increased, and that this augmentation was mainly due to excessive rapid eye movement (REM) sleep duration. Levels of serotonin, catecholamines, and their metabolites were measured in cerebrospinal fluid, and it was

found that REM sleep episodes seemed to parallel reduced homovanillic acid excretion. Several drugs, including L-dopa, 5-hydroxytryptophan, haloperidol, cyproheptadine, and clonidine were administered to determine their effects on REM sleep patterns. Results indicate that a defect of brain dopamine might exist in narcoleptic patients and that L-dopa administration could be a possible treatment of narcolepsy. 3 references.

240710 Jovanovic, U. J. Universitats-nervenklinik, 87 Wurzburg, Rontgenring 12, Germany **/Studies on sleep effects of alimemazin (Theralene).** Untersuchungen des Schlafes unter Wirkung von Alimemazin (Theralene)./ Medizinische Welt (Stuttgart). 26(25):1245-1251, 1975.

A series of tests were administered to 18 individuals with normal or disturbed sleep to assess the effects of alimemazin (Theralene) on sleep. Placebo or verum were given alternatively and their effects on sleep were polygraphically registered. Results indicate that a single 5mg dose of alimemazin had almost no influence on sleep; a 10mg dose deepened sleep; a 15mg dose shortened time of being awake and increased the soundness of sleep; and a 5mg dose three times a day normalized sleep disturbances. Patients with sleep disturbances due to neurotic or depressive symptoms felt subjective relief, whereas healthy persons experienced hangover after taking the drug. 35 references.

240711 Klich, Robert. 507 Bergisch-Gladbach, Hauptstr. 218, Germany **/Behavior disorders in childhood and their treatment.**/ Verhaltensstorungen im Kindersalter und deren Therapie. Medizinische Welt (Stuttgart). 26(25):1251-1254, 1975.

The most frequent psychosomatic disturbances in young children and children of early school age, such as sleep disorders, development disorders, headache, and constipation are described. Following an overview on the therapeutic possibilities and properties of valmane, a valerian related compound, the drug was examined in tests administered to 120 children. Results indicate that 74.4% of the cases had a positive outcome. Problems of dosage regulation and compatibility are discussed. 29 references.

240762 Deonna, Th.; de Crousaz, G.; Magrini, G.; Bechtel, P.; Schelling, J.-L. no address **/Plasma concentration of diphenylhydantoin in the epileptic: its interest for the clinician.**/ Concentration plasmatique de phenytoine chez les epileptiques – interet pour le clinicien. Schwiezerische Medizinische Wochenschrift (Basel). 105(30):936-941, 1975.

Plasma concentrations of diphenylhydantoin were determined by Wallace's method in 150 samples taken from 121 epileptic patients. They correlated well with those determined by gas chromatography, were not dose dependent and were often below 10microliters/ml. They were above 20microliters/ml in six patients with central nervous system intoxication. These determinations were also useful for detecting patients who did not take the drug as prescribed. However, blood levels did not seem to offer an accurate index of the effectiveness of diphenylhydantoin. 17 references. (Journal abstract)

240977 Becker, Robert A. Saint Louis University **Non-medication management of hyperkinetic children in the classroom. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-26225 HC$18.00 MF$7.50 74 p.

The effectiveness of substitution of a nonmedication therapy (tea or Coca Cola), in controlling hyperkinetic behaviors of preschool children and in producing equally satisfactory cognitive gains without the side-effects of methylphenidate (Ritalin) was assessed. Ss who had been diagnosed as hyperkinetic and were attending a full day Head Start or daycare center were pretested and posttested, along with a group of normal controls, on the Stanford Binet Intelligence Test, and the Cooperative Preschool Inventory. Results indicated no significant differences on intelligence, achievement gains, or behavior ratings between Ss receiving the medication and those receiving one of the nonmedication therapies (tea). The other nonmedication group (Coca Cola) apparently had little effect in controlling hyperkinetic behavior, as significant differences were reported between these Ss and children receiving medication. Some significant differences between medication and nonmedication treatment were found. Insofar as the long-term and short-term side-effects associated with a medication treatment could be eliminated with equally produced cognitive gains through use of a nonmedication therapy, serious consideration for this alternative treatment approach should be noted. (Journal abstract modified)

242212 Morselli, P. L.; Monaco, F.; Gerna, M.; Recchia, M.; Riccio, A. Istituto di Richerche Farmacologiche "Mario Negri", Via Eritrea, 62, 20157 Milan, Italy **Bioavailability of two carbamazepine preparations during chronic administration to epileptic patients.** Epilepsia. 16(5):759-764, 1975.

Two preparations of carbamazepine, as tablets and in syrup, were given for 8 weeks to 20 patients with epilepsy in a randomized crossover study. Weekly plasma levels were 3 to 21mg/l on dosages of 5 to 24mg/kg day. There were no differences in absorption or steady state level between the two preparations. Carbamazepine-10,11-oxide was constantly present when the level of carbamazepine was over 5mg/l, and tended to be lower with the syrup. 13 references. (Author abstract)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

240076 Bowers, Malcolm B., Jr. Yale University School of Medicine, 333 Cedar St., New Haven, CT 06510 **Serotonin (5HT) systems in psychotic states.** Psychopharmacology Communications. 1(6):655-662, 1975.

Lumbar cerebrospinal fluid (CSF) 5-hydroxyindoleacetic acid (5HIAA) following probenecid was negatively correlated with prognostic variables in a group of schizophrenic patients. Acute schizophrenic patients had lower CSF 5HIAA than chronic patients. CSF 5HIAA was negatively correlated with measured activity and rated agitation in a mixed group of schizophrenic patients. Evidence that lysergic acid diethylamide (LSD) directly inhibits the firing of serotonergic neurons is cited. Individuals who developed prolonged psychotic reactions following LSD ingestion had relatively good premorbid trait histories and a family history of psychosis in 33% of cases compared to 21% for nondrug induced psychotic patients. It is concluded that if central serotonin systems in man are mainly inhibitory, results are consistent with the hypothesis that in some acute psychotic states a primary decrease in serotonergic neuronal activity may contribute to excessive central nervous system arousal. 15 references. (Author abstract)

241428 Fischer, R.; Goldman, H. Maryland Psychiatric Research Center, P.O. Box 3235, Baltimore, MD 21228 **Therapeutic usefulness of hallucinogenic drugs as a function of**

their chemical structure. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 8(4):176-178, 1975.

The relationship between the therapeutic usefulness of hallucinogenic drugs and their chemical structures is discussed. D-(lysergic acid diethylamide) (LSD) displays the phenylethylamine pattern present in mescaline, cyclazocine and catecholamines and the 4 substituted tryptamine structure of psilocybin which is a serotonin analog. Therefore, it is concluded that: (a) Naloxone, a blocker of the LSD like side-effects of cyclazocine, should (and does) block effects of LSD; and (b) cross-tolerance may be present between LSD and cyclazocine, but not between mescaline and psilocybin. It is noted that even though LSD binds subcortically, its effect on regional perfusion of the brain and, presumably, function is primarily cortical and, since the perfusion shifts evoked by psilocybin are confined to subcortical regions, it is suggested that other compounds with the phenylethylamine structure such as mescaline, also may selectively affect cortical activity. 19 references. (Author abstract)

241505 Jacobs, Barry L. Dept. of Psychology, Princeton University, Princeton, NJ 08540 **Serotonin: the crucial substance that turns dreams on and off.** Psychology Today. 9(10):70-71, 1976.

The role of serotonin in regulating dreams and drug induced hallucinations is described. The induction of waking dreams in cats through the administration of parachlorophenylalanine, a serotonin blocker, is reported. A study which indicated that serotonin rich raphe neurons do not fire during rapid eye movement sleep is also cited. Application of LSD (lysergic acid diethylamide) to the raphe area slowed the firing of raphe cells, breaking the chemical blockade of hallucinations that is normally maintained by serotonin. It is proposed that the cells responsible for dreams are the target cells, such as those of the amygdala and visual system which are controlled by the serotonin rich raphe group. Visual and emotional hallucinations experienced in LSD trips are explained in terms of this hypothesis.

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

238748 Alkana, R. L.; Parker, E. S.; Cohen, H. B.; Birch, H.; Noble, E. P. Dept. of Psychiatry, University of California, Irvine, CA 92717 **L-dopa, aminophylline, ephedrine: antagonistic interaction with ethanol in humans.** Federation Proceedings. 35(3):467, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, an investigation of the relationship between the behavioral effects of ethanol and the functional capacity of brain catecholamine systems was reported. The effect of postethanol treatment with catecholamine augmenting drugs on intoxication in humans was examined. Male moderate drinkers ingested ethanol and then either L-dopa or placebo in one experiment, or aminophylline, ephedrine, aminophyline plus ephedrine, or placebo in a second experiment. A double-blind, within subjects, cross-over design was employed. Treatment with L-dopa significantly reduced ethanol's effect on neurological function, motor coordination and divided attention performance. Treatment with aminophylline and/or ephedrine also significantly reduced ethanol's effect on neurological function and motor coordination. It is suggested that the ethanol antagonism induced by these drugs results from central noradrenergic rather than general catecholaminergic stimulation, since dopaminergic augmentation reportedly increases ethanol's depressant effect. (Journal abstract modified)

238796 Whyte, Michael P. NIH, Bethesda, MD 20014 **Phenobarbital (PB) disposition in man: presumptive evidence for several metabolites.** Federation Proceedings. 35(3):565, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, phenobarbital (PB) disposition in man was reported. Para-methylphenobarbital was used as the internal standard in a urine extraction procedure with 95% recovery, followed by gas/liquid chromatography analysis, to investigate the quantitative disposition of PB to its metabolites para-hydroxyphenobarbital (PHPB) and meta-hydroxyphenobarbital (MHPB). Epileptic patients receiving chronic oral PB therapy and one male volunteer who received a single 130mg dose of PB intravenously were studied. Unaltered PB and both free and conjugated PHPB were found in the urine of all subjects. PHPB was excreted mainly as the conjugate; presumably the glucuronide since it was liberated by incubation with beta-glucuronidase but not sulfatase. MHPB was not detected in any urine sample. The urinary PB concentration generally exceeded that of the total PHPB. PB and total PHPB together accounted for only 24%-77% of the patients' daily dose of PB. In the volunteer, 30% of the initial dose was accounted for over the entire 16 day collection period. It is suggested that metabolites other than PHPB or MHPB may be of quantitative significance in the dispostion of PB in man. (Journal abstract modified)

238797 Kullberg, M. P.; Griffith, J. D. NIDA Addiction Research Center, Lexington, KY 40511 **The effects of ascorbic acid (AA) pretreatment on amphetamine (A) excretion in man.** Federation Proceedings. 35(3):565, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, the effects of ascorbic acid (AA) pretreatment on amphetamine excretion (A) in man were reported. Urinary A was determined by extraction with benzene and analysis by gas chromatography on a 3% OV-17 column using an electron capture detector. Subjects receiving AA pretreatment excreted an average of 38% less A than the same subjects receiving A alone. However, AA pretreatment produced no change in the acute pharmacological effects of A in man. Urinary pH did not account for the diminution of A excretion. Preliminary studies indicate that there was no concomitant increase in hydroxylated A metabolites, p-hydroxyamphetamine, p-hydroxynorephedrine or phenylpropanolamine to account for the decreased A excreted. (Journal abstract modified)

238997 van Praag, H. M.; Korf, J. Dept. of Biological Psychiatry, Psychiatric Univ. Clinic, Oostersingel 59, Groningen, The Netherlands **Biochemical research into psychosis: results of a new research strategy.** Acta Psychiatrica Scandinavica (Kobenhavn). 51(4):268-284, 1975.

The neuroleptics chlorpromazine, haloperidol and oxypertine were studied, and it was found that they influence central catecholamine (CA) metabolism in man. An increased central dopamine (DA) turnover was found to occur in psychotic disorders, mostly in the form of motor agitation. Chlorpromazine, with presumed ability to reduce both DA-ergic and noradrenaline (NA)-ergic transmission, and oxypertine, as a more selective blocker of NA-ergic transmission, were selected for comparison. The overall therapeutic effect of oxypertine was inferior to that of chlorpromazine, whereas oxypertine proved more effective in cases where loss of initiative was predominant. Chlorpromazine also exerted a more marked influence on extrapyramidal motor functions than oxypertine. In chronic psychotic disorders with inertia, oxypertine thus seems to be a neuroleptic which is strong enough to prevent

exacerbation of delusions and hallucinations, while at the same time increasing the level of motivation. These findings are in accordance with the predictions. 29 references. (Author abstract modified)

239305 Lake, C. R.; Ziegler, M. G.; Slater, S.; Murphy, D. L.; de la Vega, C. E. Laboratory of Clinical Science, NIMH, Bldg. 10, Rm. 2D-46, Bethesda, MD 20014 **Reduced plasma norepinephrine and dopamine-beta-hydroxylase during fenfluramine (Pondimin) treatment in man. (Unpublished paper).** Bethesda, MD, NIMH, 1976. 1 p.

The effects of fenfluramine (F), an anorexiogenic drug structurally related to amphetamine, on plasma levels of norepinephrine (NE) and dopamine-beta-hydroxylase (DBH) were investigated in six physically healthy depressed adults. During F treatment basal levels of NE decreased and levels of NE while standing also decreased. F treatment decreased basal plasma activity, and pulse and blood pressure (BP) decreased only slightly during F therapy. F treatment apparently also decreased sympathetic nervous discharge as measured by NE and DBH levels. NE levels doubled acutely when subjects stood and there was no postural hypotension. The absence of a comparable decrease in BP with F implies that very effective compensatory mechanisms were involved in these patients or that basal NE levels are not directly related to BP over a period of days. (Author abstract modified)

239658 Pitlick, William H.; Levy, Rene H.; Troupin, Allan S.; Green, John R. School of Pharmacy, University of Pittsburgh, PA 15261 **Pharmacokinetic model to describe self-induced decreases in steady-state concentrations of carbamazepine.** Journal of Pharmaceutical Sciences. 64(3):462-463, 1976.

Serum carbamazepine levels were examined during chronic administration of 6mg/kg/day for 22 days to six normal drug free volunteers. During the 3 weeks of treatment, there were significant decreases in average, maximum, and minimum (Cmin) steady state serum concentrations compared to values predicted from single dose studies in the same subjects. By the end of the third week, the average steady state concentration was 50% of the level predicted from single dose studies; elimination half-life had decreased from a single dose value of approximately 33.9hr to approximately 19.8hr. A new pharmacokinetic model is proposed, based on the observation that Cmin appears to decrease at an exponential rate during multiple dosing with carbamazepine. The close agreement of experimentally observed mean serum concentrations with concentrations predicted using the proposed self-induction model indicate that the proposed model provides an adequate mathematical description of the rate of the process of self-induction of carbamazepine during chronic administration and allows calculation of a dose regimen that will maintain constant average concentrations at steady state. 9 references.

239684 Sharples, D. Dept. of Pharmacy, The University, Manchester M13 9PL, England **Factors affecting the binding of tricyclic tranquillizers and antidepressants to human serum albumin.** Journal of Pharmacy and Pharmacology (London). 28(2):100-105, 1976.

The linear free energy related model for structure/activity relations developed by Hansch & Fujita (1964) was used to correlate the binding of tricyclic tranquilizers and antidepressants to human serum albumin (HSA) with hydrophobic and electronic parameters. The parameters chosen were the chromatographic parameter (Rm) and the affinity of charge transfer complex formation (kc). The relative importance of these factors was assessed by linear and multiple linear regression analysis. Results show that the major factor in binding is electronic, with only a minor contribution from the hydrophobic parameter. 13 references. (Author abstract)

239936 Greenberg, Alan S.; Coleman, Mary. 2419 Briarwood Rd., Baltimore, MD 21209 **Depressed 5-hydroxyindole levels associated with hyperactive and aggressive behavior: relationship to drug response.** Archives of General Psychiatry. 33(3):331-336, 1976.

The relationship between 5-hydroxyindole (5-HI) levels in blood and behavior as modified by drug therapy in a group of institutionalized retarded patients was studied. Monitoring of 5-HI levels in blood before and after drug therapy revealed depression of 5-HI levels in 83% of hyperactive patients. In those patients with low serotonin levels, elevation of 5-HI levels in blood into the normal range by administration of a variety of psychoactive agents was associated with the disappearance of the hyperkinetic syndrome. Patients who remained hyperactive continued to have low 5-HI levels. Return of hyperactivity upon withdrawal of medication in patients who were previously well controlled was associated with a fall in 5-HI levels. Medications used in the treatment of hyperactivity may be classified as to whether they usually elevate, lower, or have no significant effect on 5-HI levels in blood. 21 references. (Author abstract modified)

240054 Vendsborg, P. B.; Prytz, S. University Department of Psychiatry, Rigshospitalet, DK-2100 Copenhagen, Denmark **Glucose tolerance and serum lipids in man after long-term lithium administration.** Acta Psychiatrica Scandinavica (Kobenhavn). 53(1):64-69, 1976.

Intravenous glucose tolerance and serum lactate concentration during the tolerance test were determined in the 12 patients not suffering from a manic-depressive disorder after 6 months of placebo and after 6 months of lithium treatment. At the end of these periods, values of glucose, lactate, serum free fatty acids, and serum triglycerides were measured in fasting patients. Long-term lithium treatment had no influence on these parameters. 23 references. (Author abstract)

240802 Kirby, Marilyn J.; Turner, Paul. Department of Clinical Pharmacology, St. Bartholomew's Hospital Medical College, London EC1A 7BE, England **Do "anorectic" drugs produce weight loss by appetite suppression?** Lancet (London). 1(7959):566-567, 1976.

The action of so-called anorectic drugs in producing weight loss by appetite suppression is discussed. It is noted that a peripheral action on glucose metabolism may play an important part in the weight loss associated with treatment with some antiobesity drugs such as fenfluramine and mazindol. In therapeutic concentrations these agents increase glucose uptake into animal and human skeletal muscle. This action is distinct from their effects on central transmitters and from the reduction in food intake in animals. 12 references. (Author abstract modified)

241210 Curzon, G.; Kantamaneni, B. D.; Bartlett, J. R.; Bridges, P. K. Dept. of Neurochemistry, Institute of Neurology, Queen Square, London WC1N 3BG, England **Transmitter precursors and metabolites in human ventricular cerebrospinal fluid.** Journal of Neurochemistry (Oxford). 26(3):613-615, 1976.

To investigate the influence of the availability of the precursor amino acids on the turnover of corresponding amines in the human, the relationships between cerebrospinal fluid (CSF) tryptophan and 5-hydroxyindole acetic acid (5-HIAA)

and between tyrosine and homovanillic acid (HVA) were examined. The lack of a significant correlation between ventricular tyrosine and HVA indicated that substrate availability is not an important determinant of dopamine synthesis in the human brain. The significant correlation between tyrosine and 5-HIAA presumably simply resulted from the coexistence of significant correlations between tryptophan and 5-HIAA and between tryptophan and tyrosine. The latter correlation implied that human CSF tryptophan concentration (and therefore probably brain tryptophan concentration also) is strongly influenced by mechanisms which influence other amino acids. 27 references.

241234 Morselli, P. L.; Placidi, G. F.; Gomeni, R.; Guazelli, M.; De Lisio, G.; STanden, S.; Tognoni, G. Lab. of Clinical Pharamcology, Istituto di Richerche Farmacolgiche "Mario Negri," Via Eritrea 62 I-20157 Milan, Italy **An integrated approach for the valuation of psychotropic drug in man: I. Studies on amphetamine. Relationship between drug levels and psychophysiological measurements.** Psychopharmacologia (Berlin). 46(2):211-217, 1976.

An integrated approach for the evaluation of psychotropic drug levels in men, based on the contemporary recording of drug plasma levels, central (CNS) and peripheral responses, and performance tests, is discussed, and the effects of two different amphetamine formulations were evaluated in healthy volunteers. Relationships were observed between amphetamine initial rate of entry into the blood stream and both incidence of side-effects and rise in arterial blood pressure. Minimal thresholds for CNS (5ng/ml) and peripheral (20ng/ml) effects were also be determined. It is suggested that the personality of the subject may have some bearing on both incidence of side-effects and performance. The described methodology proved valuable in valuating psychotropic drug effects in man through a comprehensive integrated approach. 23 references. (Author abstract)

241294 Schanberg, Saul M.; Kirshner, Norman. Department of Physiology, Duke University Medical Center, Durham, NC 27710 **Serum dopamine-beta-hydroxylase as an indicator of sympathetic activity and primary hypertension.** Biochemical Pharmacology (Oxford). 25(6):617-621, 1976.

Serum dopamine-beta-hydroxylase (DBH) concentration is evaluated as an indicator of sympathetic nerve activity. The possible use of DBH activity in the study of essential hypertension is also discussed. The measurement of DBH protein by radioimmunoassay is explored. The relationship between plasma DBH concentrations and its release with norepinephrine from sympathetic presynaptic vesicles is outlined. The metabolism and half-life of DBH is discussed in relation to urinary excretions of catechol metabolites. The correlation between plasma DBH and hypertension is examined in light of clinical research. 61 references.

241730 Shull, Harrison J., Jr.; Wilkinson, Grant R.; Johnson, Raymond; Schenker, Steven. Vanderbilt University School of Medicine, Nashville, TN 37203 **Normal disposition of oxazepam in acute viral hepatitis and cirrhosis.** Annals of Internal Medicine. 84(4):420-425, 1976.

The effect of acute and chronic hepatic parenchymal disease on the elimination of oxazepam (Serax), a benzodiazepine closely related chemically and pharmacologically to diazepam, was studied on seven hepatitis patients and six cirrhosis patients. Elimination half-life and the apparent oral plasma clearance for the drug in the patients were comparable to values obtained in age matched controls. In addition, the apparent volume of distribution of oxazepam, its plasma binding, blood/plasma ratio, and the rate of urinary excretion of oxazepam, predominantly as the glucuronide, were comparable in the two groups of patients and their controls. Unlike many other sedatives, oxazepam is eliminated normally in patients with parenchymal liver disease and therefore, on pharmacokinetic grounds, seems to be an excellent sedative for use in such persons. 30 references. (Author abstract modified)

14 MECHANISM OF ACTION: BEHAVIORAL

238711 Petersen, Ronald C. Biomedical Laboratory, Edgewood Arsenal, Aberdeen Proving Ground, MD 21210 **Influence of diazepam (Valium) on human learning and memory processes.** Federation Proceedings. 35(3):308, 1976.

At the 60th annual meeting of the Federation of American Societies for Experimental Biology, a study of the nature of learning and memory deficits following varying doses of diazepam in man was reported. Four trials provided a measure of how diazepam affects the learning of new material. Following the last learning/recall trial, the subjects were tested for recall of the list at various intervals up to 24 hours. Results indicate that there were virtually no differences between the placebo group and the 0.1g/kg group either on learning or on retention over the 24 hour period. However, the 0.2g/kg group's performance was substantially depressed on learning and correspondingly on retention. Their retention curve was parallel to those of the other two groups, just significantly lower. This indicates that diazepam has its primary effect on the acquisition of new material and only a minimal effect on the retention of the material once it has been learned. (Journal abstract modified)

239029 Leutner, Victor. Gipshalden 8, 7889 Grenzach-Wyhlen 1, Germany **/Sleep and hypnotic drugs: the physiology, pharmacology and clinical aspects of sleep./** Schlaf und Schlafmittel: zur Physiologie, Pharmakologie und Klinik des Schlafes. Medizinische Welt (Stuttgart). 27(1):1-10, 1976.

The physiology of sleep, sleep regulation, and stages of sleep are discussed. Arousal mechanisms and the etiology of sleep disturbances are examined. The use and effects of various hypnotic drugs are listed: barbiturates suppress the functions of the cerebral cortex, the limbic system, and the thalamus, as well as influence vegetative processes and reduce rapid eye movement (REM) sleep; methaqualone is similar to the barbiturates but affects mostly the reticular formation and does not reduce REM sleep; benzodiazepine derivatives act as limbic system sedatives, and do not reduce REM sleep. Problems with side-effects and tolerance are examined, and the use of sedatives in the treatment of sleep disturbances, especially in old age, are discussed. 10 references.

239042 Molander, Lars; Duvhok, Christina. Clinical Research Lab., AB Ferrosan, S-201 10 Malmo, Sweden **Acute effects of oxazepam, diazepam and methylperone, alone and in combination with alcohol on sedation, coordination and mood.** Acta Pharmacologica et Toxicologica (Kobenhavn). 38(2):145-160, 1976.

Effects on critical flicker fusion frequency (CFFF), coordination and mood were studied after single oral doses of placebo, alcohol, oxazepam, diazepam, methylperone, given either alone, or simultaneously with alcohol or with delayed alcohol administration. Methylperone was found to have a depressant effect similar to or greater (on a weight basis) than that of diazepam and oxazepam, respectively. The correlation between sedative and anti-anxiety effect is discussed. The

decrease in CFFF was paralleled by a decreased coordination ability. Alcohol alone had no effect on the parameters studied but when given simultaneously with the drugs, it markedly increased the effect of diazepam, while the effect of oxazepam and methylperone were affected to a much lesser degree. The effect of the drugs on psychomotor skills and the interaction between alcohol and the drugs have important implications when treating outpatients. Methylperone as a potential anti-anxiety agent is discussed. 31 references. (Author abstract)

239058 Perkins, Richard; Baker, Martyn. Watford General Hospital, England **Changes in skin potential level during sleep in psychiatric patients.** Postgraduate Medical Journal (Oxford). 52(603):37-41, 1976.

Skin potential levels and electroencephalograph (EEG) changes were recorded in eight psychiatric patients during three nights of sleep. In a balanced design each patient took amylobarbitone sodium 200mg, chlordiazepoxide 30mg, and placebo in turn. Skin potential did not distinguish between wakefulness and sleep as measured by the EEG nor did it clearly identify individual sleep stages. Significant differences in skin potential were found between awake and stage-I, between awake and rapid eye movement (REM) sleep, and between REM sleep and stage-III/IV. The level was lowest during REM sleep but approached that of wakefulness during slow wave sleep. These findings are discussed in terms of changes in arousal threshold during sleep. A cautious comment is made on the possible effects of psychiatric diagnoses and drugs. 22 references. (Author abstract)

239059 Adam, Kirstine; Adamson, Liisi; Oswald, Ian. Dept. of Psychiatry, Edinburgh University, Morningside Park, Edinburgh, EH10 5HF, Scotland **Subjective ratings of sleep quality and anxiety after placebo, drug and a food drink.** Postgraduate Medical Journal (Oxford). 52(603):42-43, 1976.

Ten subjects (mean age 57 years) took part in a crossover study between a food drink and nitrazepam and then reported their anxiety and sleep quality. On half of the sleep laboratory nights during baseline periods, subjects were given an inert pill which they were told would improve sleep. A comparison was made between the six pill and the six nonpill nights for each subject. Subjective ratings revealed no significant difference attributable to the inert pill. Sleep quality was rated improved during both late drug and early food drink administration. On early drug withdrawal sleep quality was rated worse than baseline. 4 references. (Author abstract)

239258 Feder, Robert. University of Washington Medical School, Seattle, WA 98195 **Value of REM sleep.** New England Journal of Medicine. 294(4):227, 1976.

The value of rapid eye movement (REM) sleep is discussed, and studies on REM sleep deprivation are reviewed which indicate that in the laboratory or psychiatric ward REM deprivation results in gross deleterious effects, but it is not known what effects occur in a natural setting. It is noted that an increase in drive or motivation has been shown in depressed psychiatric patients, but the implications of the findings for nondepressed human beings have never been investigated. The REM rebound phenomenon is cited in support of the hypothesis that REM deprivation is unlikely to be without important effects. It is concluded that, while there is no compelling evidence that REM deprivation results in adverse psychological changes, a hypnotic drug that does not affect REM sleep is preferable to one that does. 2 references.

239646 Chetanasilpin, Pricha; Tuchinda, Prasertsak; Chenpanich, Krungkrei. Department of Physiology, Siriraj Hospital, Mahidol University, Bangkok, Thailand **Effects of some drugs on psychosexual response in man.** Journal of the Medical Association of Thailand (Bangkok). 58(10):509-514, 1975.

The effects of meprobamate (400mg), chlorpheniramine maleate (4mg), phenobarbital (0.5gr) and diazepam (5mg) on psychosexual responses were investigated in 10 men. With respect to placebo controls, sexual responses while looking at pictures and reading a sex book were exhibited by a significant elevation in blood pressure, both systolic and diastolic. Systolic blood pressure increased 6-26mm/Hg. Heartrate increased from 12-24 beats per minute in 8 Ss. Respiration was shallow and decreased insignificantly, 6-12 times per minute. There was no inhibition of sexual response in Ss in the drug group. The Ss complained of a feeling of drowsiness and giddiness. Blood pressure increased significantly, but changes in heart and respiratory rate were insignificant. Reading was a more potent stimulus than looking at pictures. 7 references.

239748 Laffranchini, S. Via Nassa 7, CH-6900 Lugano, Switzerland **/Five years experience in outpatient psychiatric practice with a new tranquilizer, Lexotanil (Ro 5-3350)./** Experience de cinq annees en pratique psychiatrique ambulatoire avec un tranquillisant nouveau, le Lexotanil (Ro 5-3350). Therapeutische Umschau (Bern). 32(11):741-744, 1975.

Lexotanil (bromazepam), a new benzodiazepine, was administered to 1500 patients with good results in an open trial covering a period of 5 years. In a subsequent double trial crossover comparison with oxazepam and a placebo in a total of 39 patients, the superiority of Lexotanil was clearly demonstrated. In patients treated first with Lexotanil, the target symptoms could not be further improved by the administration of oxazepam. In contrast, in cases first treated with oxazepam, Lexotanil effected further improvement. (Journal abstract)

239819 Gaillard, Jean-Michel; Tissot, Rene. Clinique psychiatrique, Universite de Geneve, CH-1225 Chene-Bourg, Switzerland **EEG sleep studies of insomniacs under flunitrazepam treatment.** International Pharmacopsychiatry (Basel). 10(4):199-207, 1975.

The effect of flunitrazepam, a new benzodiazepine, on the sleep of insomniac patients under chronic treatment was investigated. Polygraphic recordings show that this drug decreases not only the activity of the wakefulness system, but also the activity of the synchronizing system of slow wave sleep. The subjective feeling of improved and sounder sleep was related to a decrease of wakefulness pressure as well as to a decrease of body motoricity, but not with the modification of sleep stages themselves. It is suggested that flunitrazepam possesses some regulatory properties on rapid eye movement (REM) sleep, since this stage is enhanced in patients with an initial low amount of REM sleep and decreased in those having a higher initial REM sleep. It is concluded that flunitrazepam possesses potent and useful hypnogenic properties in man but does not induce physiological sleep. 19 references. (Author abstract modified)

239853 Beautrais, Annette L.; Marks, David F. Dept. of Psychology, Univ. of Otago, Dunedin, New Zealand **A test of state dependency in marihuana intoxication for the learning of psychomotor tasks.** Psychopharmacologia (Berlin). 46(1):37-40, 1976.

Cannabis cigarettes calibrated to deliver 7 mg delta9-THC were administered to experienced cannabis users and to novices in a 2 x 2 state dependency learning design using psychomotor tasks. Subjects given four training sessions under marihuana performed no better on the fifth (test) session with the drug than those subjects who had trained in the nondrug condition and were tested in the drug condition. Cannabis induced impairment in the performance of these tasks is such that prior training in the nondrug condition appears to confer no advantage to the subject. There was no evidence of state dependency effects in psychomotor performance between drug and nondrug conditions. 22 references. (Author abstract)

239992 Janos, Antal; Laszlo, Dome. Sote l. sz. Neurologiai es Pszichiatriai Klinika, Hungary **/Effect of long-lasting Trioxazin administration on the reaction time in normal individuals./** Tartos Trioxazin adas hatasa egeszseges egyenek reakcio idejere. Magyar Pszichologiai Szemle (Budapest). 32(5):513-520, 1975.

The effect of daily administration of Trioxazin for 1 and 2 weeks on the visuomotor reaction time (RT) of normal medical students was examined. It was found that RT improved slightly but significantly, in contrast to an active principle free placebo and drug free values. Even when the light signal including the reaction was projected on the peripheral retinal section, rather than on the macula, RT was improved. Prolongation and impairment of the RT of the monotonous acoustic effect was prevented by Trioxazin. Placebo did not produce these effects and the examination values of Ss treated with the drug corresponded to those of untreated persons. The role of the semilateral dominance was examined from the standpoint of occipital afferentation, an effect found considerably smaller than known for the parietal or frontal lobe. It was found that RT is impaired by the strong monotonous acoustic effect applied in the infrasound, while the normal range was impaired by the ultrasound only to a smaller degree. 12 references. (Journal abstract modified)

240074 Judd, Lewis L.; Hubbard, R. Bruce; Attewell, Paul A. Dept. of Psychiatry, School of Medicine, Univ. of California,at San Diego, La Jolla, CA 92037 **The effects of lithium carbonate upon subjective state changes induced by sodium pentobarbital.** Psychopharmacology Communications. 1(6):631-639, 1975.

The effects of lithium carbonate on subjective mood changes induced by sodium pentobarbital were investigated. Behavioral and mood changes were measured for eight normal male subjects after oral administration of sodium pentobarbital. The procedure was repeated on three occasions: first a drug free condition; then a condition following 2 weeks of maintenace on lithium carbonate; and then another drug free condition. Initial analyses indicate a lowering of the level of euphoria reached in the lithium pentobarbital condition below that achieved after pentobarbital alone. Examination of this effect showed that the reduction after pentobarbital plus lithium was mirrored by a reduction in the baseline for the same response items due to lithium alone. The lessening of euphoria appeared to result from a general lowering of affect due to lithium maintenance. More detailed analyses show that the quantitative response to pentobarbital was in no case reduced by lithium and was for certain items quantitatively increased in the lithium condition. Certain reversal effects were also discovered in which lithium plus pentobarbital acted in the opposite direction from pentobarbital alone. 6 references. (Author abstract)

240220 Schilkrut, R.; Ruther, E.; Ackenheil, M.; Eben, E.; Hippius, H. Dept. of Psychiatry, Univ. of Chile, Santiago, Chile **Clinical and biochemical parameters during neuroleptic treatment: III. Primitive reflexes during neuroleptic treatment.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 9(1):43-47, 1976.

Palmomental reflex, glabellar reflex and oral responses were studied in the course of treatment with haloperidol of 14 psychotic patients with chronic organic brain damage. An increase in the three responses was found; maximum intensity and frequency of the primitive reflexes were reached during the first 5 days of treatment. There was no correlation found between the intensity of primitive reflexes and changes of psychopathological symptoms, of extrapyramidal scores and of homovanillic acid and 5-hydroxyindoleacetic acid concentration in cerebrospinal fluid. The presence of primitive responses is interpreted as a decompensation phenomenon induced by neuroleptics, probably in relation to an effect on the central nervous system dopamine receptors. It is suggested that the appearance of several definite, primitive reflexes during neuroleptic therapy may have some diagnostic and prognostic significance. 30 references. (Author abstract)

240475 Dodrill, Carl B. Dept. of Neurological Surgery, University of Washington School of Medicine, Seattle, WA **Effects of sulthiame upon intellectual, neuropsychological, and social functioning abilities among adult epileptics: comparison with diphenylhydantoin.** Epilepsia (Amsterdam). 16(4):617-625, 1975.

In a double-blind study which compared sulthiame with diphenylhydantoin as primary agents in the treatment of uncontrolled epileptics, assessments of intellectual, neuropsychological, and social functioning abilities were made with 22 adult epileptic patients. The results show significantly less impairment with treatment by diphenylhydantoin than by sulthiame, and substantial differences were revealed on intellectual tasks, tasks calling for sustained concentration and attention, and psychomotor problem-solving tasks. The results could not be explained on the basis of increased tonic/clonic seizures while on sulthiame, however an increase in other types of seizures was noted, as was an increase in electroencephalogram (EEG) epileptiform discharges. Possible mechanisms for the decrement in performance are discussed, and the value of an objective assessment of the psychological effects of anticonvulsant agents is noted. 27 references. (Author abstract)

240644 Baumler, Gunther. Technische Universitat, Connollystrasse 32, 8 Munich 40, Germany **/Influence of psychopharmaceuticals on achievement motivation: III. Differential influence on content categories./** Beeinflussung der Leistungsmotivation durch Psychopharmaka: III. Differentielle Beeinflussung der Inhaltskategorien. Zeitschrift fur Experimentelle und Angewandte Psychologie (Gottingen). 22(4):535-546, 1975.

An analysis of the effects of two drugs, the stimulant Ritalin and the neuroleptic Megaphen, on the contents of the responses to the Heckhausen thematic achievement motivation test brought to light the usefulness of dividing the contents into two parts, the emotional content and the content dealing with activities and goal orientation. Both these drugs increased motives of success oriented activity. Accordingly, the activity oriented "net hope" increased significantly. Positive emotional states were significantly affected positively through Ritalin and negatively through Megaphen. Megaphen decreases the total number of emotional states reported by the subjects. In the case of the activity oriented contents, the male subjects

showed significantly higher "net hope" than the female subjects, mostly because the female subjects showed a stronger failure oriented attitude, although they reported fewer negative emotional states. 5 references. (Journal abstract)

240645 Dittrich, Adolf. Psychiatrische Universitatsklinik, Postfach 68, CH-8029 Zurich, Switzerland **/Comparison of altered states of consciousness induced by short sensory deprivation and by (-)-delta9-trans-tetrahydrocannabinol./** Vergleich veranderter Bewusstseinszustande induziert durch kurzdauernden Reizentzug und (-)-delta9-trans-Tetrahydrocannabinol. Zeitschrift fur Experimentelle und Angewandte Psychologie (Gottingen). 22(4):547-560, 1975.

A study comparing altered states of consciousness induced by sensory deprivation and by (-)-delta9-trans-tetrahydrocannabinol (THC) using a placebo control group is reported. Thirty-six subjects experienced one hour of sensory deprivation, darkness and white noise, 24 were given THC (250 microg/kg) and 12 were given placebo under double-blind conditions. Results indicate that both the THC and sensory deprivation produced more visual hallucinations than did the placebo. Auditory hallucinations occurred more often in the sensory deprivation setting than in the THC or placebo situation. In the scales "impairment of attention", "anxious depressive state" and "changes in body image" no differences between sensory deprivation and THC were found. In depersonalization and derealization syndromes the differences between all three were statistically significant. THC produced more such experiences than did sensory deprivation, which in turn had a greater effect than the placebo. 23 references. (Journal abstract)

240741 Konig, Liesbeth. Neurologisch-Psychiatrische Klinik, Medizinischen Akademie "Carl Gustav Carus", 8019, Dresden, Fetscherstr. 74, Germany **/Lithium tremor -- combination treatment with beta-receptor blockers?/** Lithiumtremor -- Kombinationsbehandlung mit Beta-Rezeptorenblockern? Psychiatrie, Neurologie und Medizinische Psychologie (Lepigzig). 27(2):720-724, 1975.

Different types of tremors are described with emphasis on lithium tremor. Experiences gathered from the application of beta-receptor blockers in regard to the lithium tremor are reported. Theories on the etiology and mechanism of action of this type of tremor are outlined. 25 references. (Journal abstract modified)

240831 Bigelow, George; Griffiths, Roland; Liebson, Ira. Department of Psychiatry, Baltimore City Hospitals, Baltimore, MD **Experimental human drug self-administration: methodology and application to the study of sedative abuse.** Pharmacological Reviews. 27(4):523-531, 1975.

Sedative self-administration by volunteer human Ss was investigated and discussed with respect to methodology and applications to the study of sedative abuse. The drugs available for self-administration during a 7 hour daily session were diazepam and sodium pentobarbital. Variation of the response cost per dose had a similar effect upon the self-administration of sedatives by both subjects: as cost increased, drug intake decreased. At the lowest cost level (one token per dose) both Ss consumed all or nearly all of the available doses. However, at increasing cost levels, drug intake progressively decreased in both Ss. Thus, cost was shown to be a potent environmental determinant of sedative self-administration by human sedative abusers. It is suggested that stability and sensitivity of drug self-administration behaviors are an essential prerequisite to systematic experimental analysis of human sedative self-administration determinants. 27 references.

241133 Brandman, Edward Stephan. Hofstra University **A test of the state dependent learning effects of methylphenidate in hyperactive children. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-25491 HC$18.00 MF$7.50 132 p.

The state dependent learning effects of the psychostimulant drug methylphenidate as used by hyperactive children were assessed in Ss ranging in age from 7 to 12 years and ranging in intelligence from average to bright normal. A visual/motor sequencing task in which the S reproduced from memory a sequential series of taps as demonstrated by E (Knox Cubes task from the Arthur Point Scales of Performance Task), a paired-associate task with picture items selected from the Peabody Picture Vocabulary Test, and a cross-modality task consisting of a paired-associate task presented in the visual modality during acquisition learning and in the haptic modality during recall were used. State dependent learning was observed on the Knox Cubes Task, but not on the other two tasks. The dissociation effect on the Knox Cubes Task was asymmetrical and occurred when the change in drug states was from methylphenidate to placebo. The predicted drug effects were not supported. The observation of asymmetrical state dependent learning is discussed in terms of the skills which were involved in the performance of tasks, and their apparent sensitivity to changes in drug states. Possible reasons for failure to observe dissociation effects on the other two tasks, to show relationships on the chronicity factor and state dependent learning, and to indicate drug effects are also suggested. (Journal abstract modified)

241273 Momose, Takashi; Ishii, Susumu; Kuge, Teruyoshi. Dept. of Anesthesiology, Nagoya National Hospital, Nagoya, Japan **Controlled comparison of estazolam and nitrazepam as hypnotics on the preoperative night sleep.** Current Therapeutic Research. 19(3):277-291, 1976.

A controlled, double-blind study of the efficacy of estrazolam on preoperative night sleep (on 1139 Ss) is reported. Results indicate that estazolam was effective in improving the sleep on the peroperative night. When this drug was compared with nitrazepam used as the control drug in respect to the results of global assessment of the state of sleep, the following sequence of efficiacy was proved, listed in order of most effective to least effective: estazolam 4mg; estazolam 3mg, nitrazepam 10mg and estazolam 2mg (equally effective); nitrazepam 5mg; estazolam 1mg and placebo (equally effective). The incidence of side-effects was positively correlated to drug dosage efficacy. In view of the efficacy of estazolam and the incidence of side-effects, it is concluded that the optimal dose of estazolam for improving sleep on the preoperative night is 2mg. However, it appeared that 3mg of estazolam would be required for patients with severe anxiety. 15 references. (Author abstract modified)

241274 Kasich, Anthony M.; Richards, David J.; Vanov, Svetislav K. 242 E. 72nd St., New York, NY 10021 **Lorazepam in the management of anxiety associated with chronic gastrointestinal disease: a double-blind study.** Current Therapeutic Research. 19(3):292-306, 1976.

The efficacy of lorazepam in the relief of anxiety associated with gastrointestinal disorders was compared to that of placebo and a standard active drug, diazepam, in a double-blind study of 120 patients. The patients were divided into three balanced and parallel treatment groups. Results show that lorazepam was a useful adjunct in the management of chronic gastrointestinal disease with anxiety. It was comparable to diazepam and superior to placebo in overall anti-anxiety

activity, it was well accepted and tolerated by the majority of patients, and was compatible with concomitant medications. Mild and transient sedation was the most frequent side-effect seen with both active drugs. This study also showed that, despite a high placebo response, it was possible to demonstrate the effectiveness of an active drug. 16 references. (Author abstract)

241276 Galli, G. Surgery Dept., Ospedale Generale Provinciale of Bollate, Milan, Italy **Camazepam (SB/5833) in preparation for endoscopy inspection: open and double-blind study versus diazepam.** Current Therapeutic Research. 19(3):316-319, 1976.

Camazepam (SB-5833) was investigated in an open and in a double-blind study during endoscopy inspection. The aim of the open study was to gain experience in the use of camazpeam in this field, and the double-blind trial versus diazepam was performed in order to compare the new drug with a very established drug in this field. Camazepam was administered per os in a single dose of 20mg. The parameters considered in evaluating the trial were patient's cooperation and visceral reflexes. Camazepam appeared active and more useful than diazepam during endoscopy insepection. Particularly, it does not cause drowsiness (significantly present in the group treated with diazepam) and does not interfere with secretion and peristalsis. 7 references. (Author abstract)

241474 Wyatt, Richard Jed; Gillin, J. Christian; Stoff, David M.; Moja, Egidio A.; Tinklenberg, Jared R. Lab. of Clinical Psychopharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Beta-phenylethylamine (PEA) and the neuropsychiatric disturbances. (Unpublished paper).** Washington, DC, NIMH, 1976. 39 p.

The literature on the relationship between beta-phenylethylamine (PEA) and neuropsychiatric disorders is reviewed. It is noted that PEA, the parent of several of the neurotransmitters, may produce many effects in the nervous system. Under usual circumstances, the level of PEA in the brain is extremely high, but its function in the brain is not known. It has been hypothesized that there is a disorder which is caused either by a deficiency or excess of PEA, but this has not been established. The resemblance of PEA in its pharmacological effects to amphetamine is discussed, and it is suggested that many of the chemical, pharmacological, and behavioral effects of amphetamine also occur with PEA. 99 references.

242151 Miller, Andrew Foster, Jr. Arizona State University **State dependent (dissociative) effects of methadone on human retention. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-6118 HC$18.00 MF$7.50 96 p.

The state dependent effects of methadone on human retention were examined in 30 patients at the Valle Del Sol Narcotic Prevention Project. Ten of the Ss were in methadone maintenance treatment, 10 in methadone detoxification, and 10 were drug free exheroin users. Three memory tasks (word recall, picture arrangement, and four way picture choice) were taught to the subjects to a 100% criteria level. Two weeks after the learning session the 30 subjects were tested as to their recall of the three tasks. The methadone to methadone group and the drug free to drug free groups were significantly different from the methadone to placebo group on the four way picture choice and the picture arrangement tasks. Results are interpreted as evidence of state dependent learning in these Ss. (Journal abstract modified)

242502 Leickert, K. H. 7889 Grenzach, Schlossweg 6, Germany **/Flurazepam, a new hypnotic for the treatment of insomnia./** Flurazepam -- ein neues Schlaftherapeutikum. Medizinische Welt (Stuttgart). 25(48):2021-2026, 1974.

The use of flurazepam in the treatment of insomnia is discussed, and several aspects of sleep research are reviewed. The characterization of sleep habits, the assessment of the effectiveness of sleep therapy, physiological and biochemical correlates of sleep, and the methodology of sleep monitoring are considered. It is noted that the results of electroencephalographic, electrooculographic, and electromyographic investigations indicate that flurazepam sleep is very similar to normal physiological sleep. Flurazepam reduces sleep latency and permits a 7-8 hr sleep period without altering the patterning of rapid eye movement sleep. Patients prefer flurazepam to other soporifics, as intermittent waking periods are briefer and less frequent and side-effects are minimal with no reported "hangover" effects. It is recommended that dosage be adjusted individually from 15 to 60mg at bedtime; the average nightly adult dose is 30mg. Dependence on flurazepam has not been reported. 79 references.

242702 Zingerman, A. M.; Sivokhina, N. V. Institut eksperimental'noy meditsiny AMN SSSR, Leningrad, U.S.S.R. **/Analysis of the discrepancy in "man-machine" tracking systems under conditions of delayed feedback./** Analiz rassoglasovaniya v sledyashchikh sistemakh "chelovek-mashina" v usloviyakh zaderzhannoy obratnoy svyazi. Voprosy Psikhologii (Moskva). No. 6:100-102, 1975.

The effect of delays in the chain of visual feedback on the quality of operation of automated man/machine complexes was investigated under conditions of one dimensional tracking of the movement of a point on a predictable and a nonpredictable trajectory. Results confirmed the conclusions in the literature on the dependence of the quality of regulation on the predictability to the signal and the magnitude of interval of the delays in the visual feedback chain. The findings indicate that the worsening of operator activity under conditions of the nonpredictability of the trajectory of movement of the object and delays in the feedback chain was caused by an increase in errors in the dispersion process for which it was difficult to compensate. The results of the series of trials initiated with the administration of a dose of 0.01g of phenamine to the subjects affirmed the favorable effect of the drug on the operators. In particular, it strengthened the tendency of operators to anticipate actions. 4 references.

15 TOXICOLOGY AND SIDE EFFECTS

238855 Doepp, Stefan; Buddeberg, Claus. Psychiatrische Universitatsklinik, CH-8000 Zurich, Switzerland **/Extrapyramidal symptoms under clozapine: a casuistic contribution./** Extrapyramidale Symptome unter Clozapin: ein kasuistische Beitrag. Nervenarzt (Berlin) 46(10):589-590, 1975.

The use and effects of clozapine (Leponex), a benzodiazepine derivative, in a case of chronic paranoid schizophrenia are discussed. Two attempts at treatment with clozapine of this previously neuroleptically treated patient resulted in a strengthening of the existing perioral dyskinesia. After removal of clozapine, previous symptoms returned. These results suggest a connection between the anticholinergic and dopamine like affects of clozapine. 9 references.

238862 Danke, F. Universitats-Nervenklinik, Fuchsleinstrasse 15, 87 Wurzburg, Germany **/Methylphenidate addiction -- effect reversal in withdrawal./** Methylphenidatsucht -- Wirkungsumkehr im Entzug. Psychiatria Clinica (Basel). 8(4):201-211, 1975.

A case history of a prolonged Ritalin (methylphenidate) addiction (18 years) is given, and the symptoms and the diagnostic categorization are described. Atypical withdrawal symptoms, including restlessness, sleep disturbances and depression, were observed. It is suggested that these withdrawal symptoms are an expression of a reversal of effect on withdrawal in the sense of a continuing, independent manifestation of counterregulatory, protective and specific mechanisms. 32 references. (Journal abstract modified)

238977 Dunner, David L.; Meltzer, Herbert L.; Schreiner, Helen C.; Feigelson, Janet L. Dept. of Internal Medicine, New York State Psychiatric Institute, 722 W. 168th St., New York, NY 10032 **Plasma and erythrocyte magnesium levels in patients with primary affective disorder during chronic lithium treatment.** Acta Psychiatrica Scandinavica (Kobenhavn). 51(2):104-109, 1975.

Plasma and erythrocyte magnesium concentrations were measured in 79 clinic outpatients who had histories of bipolar or unipolar primary affective disorder and who were being chronically treated with lithium carbonate (60 patients) or placebo (19 patients). Although slight differences in the mean concentration of magnesium in plasma and erythrocytes were noted with lithium treatment, diagnosis, and sex, the differences overall failed to achieve statistical significance. In contrast to prior reports demonstrating increases in plasma magnesium during acute lithium carbonate treatment of affectively ill patients, these data suggest that the prelithium steady state is achieved during chronic lithium treatment. 17 references. (Author abstract)

238978 Martin, Ian C. A. Memorial Hospital, Darlington DL3 6HX, England **Implications of phenothiazine side effects: a study of antiparkinsonian agents in an older population.** Acta Psychiatrica Scandinavica (Kobenhavn). 51(2):110-118, 1975.

Antiparkinsonian agents in prolonged phenothiazine therapy were examined to clarify some anecdotal misconceptions. It was found that antiparkinsonian agents do not affect the therapeutic efficiency of phenothiazines, nor does using them on a "demand" basis increase the problems of control of parkinsonian side-effects. Older patients, however, required the extended usage of antiparkinsonian agents rather more than some other studies suggest. It is suggested that sustained release antiparkinsonian agents may further simplify the management of schizophrenia. 9 references. (Author abstract modified)

238998 Jeppsson, J.; Sjogren, J. Dept. of Pharmacy, Hassle Ltd., Fack, S-431 20 Molndal 1, Sweden **The influence of food on side effects and absorption of lithium.** Acta Psychiatrica Scandinavica (Kobenhavn). 51(4):285-288, 1975.

In a crossover study, 24 mmol of lithium sulfate was given as a single dose in slow release tablets to 30 healthy volunteers fasting and after a standardized meal. Comparisons were also made with lithium citrate in slow release tablets and placebo. Postprandial administration of lithium gave practically no side-effects, while lithium on an empty stomach gave diarrhea in about 20% of the subjects. The absorption was measured by determination of the amount of lithium excreted in the urine in a group of 10 subjects. Lithium was completely absorbed when given after food, but when given on an empty stomach the absorption was lower in some subjects, apparently due to rapid gastrointestinal passage in connection with diarrhea. Lithium should therefore preferably be administered after meals. 8 references. (Author abstract)

239001 Patch, I. C. Lodge. Springfield Hospital, Beechcroft Rd., London SW17 7DJ, England **Pigmentation and the chemical basis of schizophrenia.** Acta Psychiatrica Scandinavica 51(5):312-318, 1975.

Using a Lovibond flexible fibrooptic tintometer, no differences of skin pigmentation were found between chronic male schizophrenic patients untreated with phenothiazines, and nonschizophrenics. No differences were found between chronic male schizophrenics receiving phenothiazines and those not so treated. This latter comparison may, however, be questioned on the grounds that the treatment had consisted not of chlorpromazine alone (which is particularly associated with pigmentation), but of a variety of drugs, including fluphenazine. No support is provided for the hypothesis proposed by Greiner and Nicholson linking the supposed chemical basis of schizophrenia with pigmentation. 13 references. (Author abstract)

239010 Sambrooks, Jean E.; MacCulloch, M. J.; Rooney, J. F. F. Dept. of Psychiatry, Univ. of Liverpool, 6 Abercromby Sq., P.O. Box 147, Liverpool L69 3BX, England **The automated assessment of the effect of flurazepam and nitrazepam on mood state.** Acta Psychiatrica Scandinavica (Kobenhavn). 51(3):201-209, 1975.

The effects of two hypnotic drugs, nitrazepam and flurazepam monohydrochloride, on mood state are described. An automated assessment and scoring system, Computer Assisted Psychometric System (CAPS), was used to assess mood state and showed that both hypnotics had a mild euphoriant effect even when administered to healthy volunteers during the daytime. This was most marked in the case of nitrazepam. It is argued that such euphoriant side-effects should be further investigated as they can occur when hypnotics are administered on a long-term nightly basis, and there may therefore be a dependency aspect for those patients who habitually take such hypnotic drugs. The broad scope of the CAPS system is also discussed. 13 references. (Author abstract)

239682 Jacobi, P.; Maxion, H. H. Klinikum der J. W. Goethe Universitat, Abteilung fur Neurologie, 6 Frankfurt/M-71, Schleusenweg 2-16, Germany **/Psychometric effects of perphenazine below the "neuroleptic threshold."/** Psychomotorik vor Erreichen der neuroleptischen Schwelle Untersuchungen nach Gabe von Perphenazin. Pharmakopsychiatrie Neuro-psychopharmakologie (Stuttgart). 8(6):366-374, 1975.

In order to evaluate methods of assessing the extrapyramidal/motorical side-effects of neuroleptic drugs, the results of the handwriting test (Hasse, 1969) were compared with electromyographic measurements of the silent period and psychometric measurement of aiming, tapping, and reaction time tests. Twenty normal subjects were tested four times in a double-blind study in order to control the short-term and long-term effects of a low dosage of perphenazine. Slight but significant drug dependent changes were found, such as decreases of steadiness and of the speed of arm/hand movements. From the theoretical point of view these results support a dimensional approach rather than an explanation in terms of a categorial approach, as suggested by the commonly used notion "neuroleptic threshold." 20 references. (Author abstract modified)

239695 Ferrari, E. Clinica per le Malattie Nervose e Mentali, Universita di Bari, Italy **/Problems involved in administering L-dopa./** Problemi posti dall'uso della L-dopa. Rivista di Patologia Nervosa e Mentale (Firenze). 95(4):239-250, 1974.

At the Symposium on Central Nervous System Neurotransmitters, held in Rome, December 1973, the side-effects of dopaminergic treatment were discussed based on a review of the literature. The side-effects include neurovegetative phenomena connected to the catecholaminergic effects of products of the peripheral or central catabolism of L-dopa. The strikingly different vegetative, extrapyramidal and psychological phenomena (in particular disturbances in vigilance and mood tone) could be interpreted within the framework of a unitary conception which postulates substantially similar functional modalities in the neurobiological substrates which underlie the neurovegetative phenomena (dystonia) and the extrapyramidal (muscular "tone") and psychological (mood tone, vigilance) phenomena. Monoaminergic and cholinergic neurons (within a range of reciprocal balanced, though unstable equilibrium) appear to underlie (with a similar modality of action at progressively higher levels of integration) the various functions involved in dopaminergic treatment. 25 references. (Journal abstract modified)

239782 Hertrich, O. Rosenheimer Strasse 2, 8 Munich 80, Germany **/Therapy of psychopharmaceutical side-effects with distigminbromide (Ubretid, BC 51)./** Therapie psychopharmakabedingter Nebenwirkungen mit Distigminbromid (Ubretid BC 51). Nervenarzt (Berlin). 46(5):264-267, 1975.

Pharmacotherapeutic characteristics of the cholinesterase inhibitor distigminbromide (Ubretid BC-51) are discussed. The drug has a 24 to 36 hour effectiveness and is easily tolerated. In general medical practice it is useful in cases of bladder and intestinal atonia. In neurology it is used in the long-term treatment of myasthenia gravis pseudoparalytica. In psychiatry it is a useful addition to neuroleptic and thymoanaleptic therapy where it counteracts psychopharmaceutical side-effects such as mouth dryness and accommodation disturbances. Generally, 5 to 10mg per day are sufficient. Examination of the ganglioplegic effects on psychoses shows that the lessening of the cholinergically determined side-effects does not diminish the pharmacological influence on the psychoses. 15 references.

239783 May, Volkmar. Landeskrankenhaus fur Psychiatrie u. Neurologie Klosterneuberg, A-3412 Klosterburg, Austria **/Therapeutic combination of psychopharmaceuticals and beta-adrenergic blockers./** Therapeutische Kombination von Psychopharmaka und Beta-Sympathicolytica. Nervenarzt (Berlin). 46(5):268-271, 1975.

The use of the beta-adrenergic blocker prindolol (Visken) is discussed. Indications include cases of tachycardia resulting from the thymoleptic treatment of depressive psychoses, from neuroleptic treatment of schizophrenia and mania, and from results of misuse of alcohol and drugs. In all cases the use of prindolol lowers the pulse rate. Electrocardiograph studies reveal no significant side-effects. It is concluded that beta-adrenergic blockers may be useful in the long-term combination therapy of chronic psychoses. 7 references.

239822 Fleischhauer, J. Psychiatrische Universitatsklinik, Wilhelm-Klein-Strasse 27, CH-4000, Basel, Switzerland **Open withdrawal of antiparkinson drugs in the neuroleptic-induced Parkinson syndrome.** International Pharmacopsychiatry (Basel). 10(4):222-229, 1975.

Results of open withdrawal of antiparkinson drugs on neuroleptic induced Parkinson symptoms are reported. None of the 32 patients who completed the study had to be given another antiparkinson treatment due to reappearing Parkinson symptoms. Slight and constant deterioration in their condition occurred in four patients within 1-3 weeks following withdrawal of the antiparkinson medication, and this fact justified recommencement of the antiparkinson therapy. All but seven patients had been given antiparkinson drugs for more than 1 year. All patients were on neuroleptic drugs. The neuroleptic dose was increased in seven patients, a slight transient deterioration of the Parkinson symptoms occurring in two cases. Investigation into the longitudinal course of the diseases revealed that the intensity of symptoms is not always steady, but that certain variations occur. An equable course was observed in paranoid schizophrenics. In cases of catatonia and hebephrenia, variations in the symptoms and their intensity are expected, but these variations need not inevitably call for recommencement of the antiparkinson treatment. Results confirm similar available studies in that the incidence of relapses in cases of neuroleptically conditioned Parkinson's disease was very low (8%) in patients who had been receiving antiparkinson medication for long periods. 4 references. (Author abstract modified)

239835 Gabriel, E.; Karobath, M.; Lenz, G. Psychiatrische Universitatsklinik, Lazarettegasse 14, A-1090 Vienna, Austria **/Extrapyramidal symptoms in a combination of lithium long-term therapy with nortripytline: a causistic report on pathogenesis and hypothesis formulation./** Extrapyramidale symptomatik bei Kombination der Lithium-Langzeittherapie mit Nortripytlin: ein kasuistischer Beitrag zu Pathogenese-Hypothesenbildung. Nervenarzt (Berlin). 47(1):46-48, 1976.

The treatment of a patient with manic-depressive psychosis is discussed in which combined therapy with a lithium preparation and nortriptyline led to unexpected parkinson-like extrapyramidal symptoms. The possible biochemical determinants of this particular individual sensitivity to the combined treatment is discussed, and it is postulated that the onset of extrapyramidal symptoms may have been due to a synergistic effect of the lithium and the nortriptyline on a normally functional, but damaged, striatum. 12 references.

239943 Charuvastra, Charles V.; Panell, Jan; Hopper, Michael; Erhmann, Mary; Blakis, Mara; Ling, Walter. Dept. of Psychiatry, University of California, Los Angeles, CA 90024 **The medical safety of the combined usage of disulfiram and methadone: pharmacological treatment for alcoholic heroin addicts.** Archives of General Psychiatry. 33(3):391-393, 1976.

The results of hematology and blood chemistry tests were examined in eight methadone maintenance patients who had been treated concurrently for alcoholism with disulfiram (Antabuse). There were no apparent major differences between the results of tests run prior to the initiation of the disulfiram treatment and subsequent tests run up to 16 months after treatment was begun. There was a trend toward normalization of serum glutamic oxaloacetic transaminase (SGOT) values. The results suggested no contraindications to this combined pharmacological treatment. 11 references. (Author abstract)

240048 Rasmussen, K.; Kirk, L.; Faurbye, A. Department of Ophthalmology, Roskilde County Hospital, Roskilde, Denmark **Deposits in the lens and cornea of the eye during long-term chlorpromazine medication.** Acta Psychiatrica Scandinavica (Kobenhavn). 53(1):1-6, 1976.

Thirty patients on long-term treatment with chlorpromazine in moderate doses were examined to determine a possible causative relationship between the drug and pigment deposits in the lens and cornea of the eye Pigment deposits in the lens were found in all 30, and the majority of the patients also showed deposits in the cornea. The deposits did not increase

in 13 patients who continued on chlorpromazine during an observation period of 3.5years. It is suggested that when chlorpromazine is used in moderate doses, the deposits in the eyes seem to increase only up to a certain extent. Twelve patients who were switched over to thioridazine showed no change in the deposition in the lens and cornea after the observation period, indicating that the deposits are irreversible. After the observation period, visual acuity had deteriorated somewhat in the material as a whole, presumably because of advancing age, not because of the deposits. It is concluded that the risk of using chlorpromazine in moderate dosage is slight. 10 references. (Author abstract modified)

240243 Goodson, William H., Jr.; Litkenhous, Edward E., Jr. Huntsville-Madison County Mental Helath Center, 660 Gallatin St. S.W., Huntsville, AL 35801 **Sudden unexplained death in a psychiatric patient taking thioridazine.** Southern Medical Journal. 69(3):311, 315, 320, 1976.

The sudden unexplained death of a young, physically healthy, psychotic woman, who had received moderate doses of thioridazine for 4 days prior to her death, is described. No cause of death could be determined at autopsy. The literature regarding other such case reports and possible cardiotoxic effects of phenothiazine is cited, but no clear cut correlations or explanations have been demonstrated. 10 references. (Author abstract modified)

240251 Mayer, Doris Y. Nazeing Park School for Maladjusted Children, Cambridge, England **Psychotropic drugs and the 'anti-depressed' personality.** British Journal of Medical Psychology (London). 48(4):349-357, 1975.

The psychological effects of psychotropic drugs are discussed. The relative efficacy of these drugs is disputed and it is argued that they are overprescribed by physicians and overpromoted by drug companies. Three dangers of overuse of these drugs are cited: 1) the increase in iatrogenic disease; 2) the loss of the protective function of unpleasant feelings; and 3) the dehumanization resulting from the loss of emotional experience. It is charged that psychotropic drugs tend to create an antidepressed personality, which is defined as one who is devoid of feelings and emotions. 29 references.

240261 Hollstein, H. Nervenkrankenhaus, 877 Lohr, Germany **/Astonin-H in the treatment of arterial hypertension due to psychotropic drugs./** Astonin-H bei der Behandlung psychopharmackabedingter hypotoner Kreislaufregulationsstorungen. Medizinische Welt (Stuttgart). 26(6):231-233, 1975.

Twenty women with hypertension resulting from psychopharmaceutical treatment were treated with 9alpha-fluorohydrocortisone (Astonin-H). In 14 cases a dosage of 0.2-0.4mg/day resulted in an improvement in subjective condition and objective measurements within 4 to 8 days. The effective maintenance dosage was 0.1-0.2mg. The only observed side-effect was edema in six cases. 3 references.

240473 Dodrill, Carl B. Dept. of Neurological Surgery, University of Washington School of Medicine, Seattle, WA 98195 **Diphenylhydantoin serum levels, toxicity, and neuropsychological performance in patients with epilepsy.** Epilepsia (Amsterdam). 16(4):593-600, 1975.

The neuropsychological effects of diphenylhydantoin were assessed in 70 adults having primarily psychomotor and major motor seizures. All patients were stabilized on diphenylhydantoin alone, and assessment of this drug by gas/liquid chromatography provided a basis for dichotomizing the group into high and low drug groups, both with and without toxic patients. Patients showing signs of toxicity were contrasted with those not showing such signs. In each of these comparisons, control was maintained with respect to the variables of age, education, age at onset of disorder, and duration of disorder. Results show that the high and toxic groups rather consistently did more poorly on all tasks than the low and nontoxic groups. Differences which were statistically significant appeared only in connection with tasks which had a heavy motor component. Possible reasons for the lack of statistically significant differences on the higher level mental tasks are discussed. 11 references. (Author abstract)

240692 Janzik, H.-H.; Mayer, B.; Petruch, F. Neurologische Klinik und Poliklinik der Universitat, 7400 Tubingen, Liebermeisterstrasse 18-20, Germany **/DPH-intoxication -- clinical and neuropsychological evaluation of a slow DPH-elimination./** DPH-Intoxication -- Klinische und neuropsychologische Befunde bei einer extrem langsamen Diphenylhydantoin-Elimination. Medizinische Welt (Stuttgart). 26(2):79-81, 1975.

A case history of diphenylhydantoin (DPH) intoxication is discussed and the neurotoxic and neuropsychological symptoms present are noted. After 1 year of DPH administration the patient's reactions to the drug were monitored by means of various psychiatric and clinical tests. After a severe case of nystagmus, gait disturbances and dissequilibrium the drug was discontinued. The relationship between DPH intoxication and cerebral dysfunction and metabolic problems is discussed. 11 references.

240697 Goswami, S. N. 613 Borla Co-operative Housing Society, Bombay, 400 074 India **Phenothiazine-jaundice (a review).** Maharsahtra Medical Journal (Poona). 21(8):285-290, 1974.

Incidence, pathology and treatment of chlorpromazine induced jaundice are discussed, and clinical evidence of the jaundice inducing potential of other phenothiazines is presented. Usually no specific treatment of the phenothiazine induced icterus is necessary or is available. The most important measure to be taken is the immediate withdrawal of the offending phenothiazine. It is recommended that patients be treated as those suffering from cholestatic jaundice, and that antipsychotic treatment be undertaken with nonphenothiazine neuroleptics. 18 references.

240843 Goodman, Jay M.; Bischel, Margaret D.; Wagers, Park W.; Barbour, Benjamin H. Dept. of Medicine, Los Angeles County/University of Southern California Medical Ctr., Los Angeles, CA **Barbiturate intoxication: morbidity and mortality.** Western Journal of Medicine. 124(3):179-186, 1976.

Complications encountered in caring for 185 patients intoxicated with barbiturates are reviewed. The population consisted of 142 patients with long-acting barbiturate concentrations of 8mg per 100ml or greater, 20 patients with short acting barbiturate concentrations of 3mg per 100ml or greater, and 23 consecutive patients with short acting barbiturate intoxication referred for monitoring. Pneumonia was the major cause of morbidity and mortality and correlated best with the initial depth of coma and the use of an endotracheal tube in treatment. Cardiovascular instability manifested by pulmonary edema was the next leading cause of morbidity and morality and correlated best with the initial depth of coma and the quantity of intravenous fluid administered. In retrospect, use of eliminative measures such as dialysis would probably not have altered the outcome in most of the patients who died, and attempts at forced diuresis may have contributed to

several deaths. It is concluded that particular emphasis should be placed on the problems of sepsis and fluid therapy in the management of these patients. 34 references. (Author abstract)

241357 Jeong, Yune-Gill; Caccamo, Leonard P. Dept. of Internal Medicine, St. Elizabeth Hospital, 1044 Belmont Ave., Youngstown, OH 44505 **Amitriptyline poisoning causing left bundle branch block.** Ohio State Medical Journal. 72(4):217-219, 1976.

A patient with mental depression developed transient left bundle branch block (LBBB) secondary to an amitriptyline hydrochloride intoxication as a suicidal attempt. A review of the literature uncovered six additional cases of LBBB during amitriptyline hydrochloride intoxication or treatment. Amitriptyline hydrochloride poisoning or treatment has been associated with electrocardiogram changes of transient autonomic dysfunction and, in several incidents, even sudden death. 12 references. (Author abstract)

241417 Saario, I.; Linnoila, M. Dept. of Pharmacology, Univ. of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Effect of subacute treatment with hypnotics, alone or in combination with alcohol, on psychomotor skills related to driving.** Acta Pharmacologica et Toxicologica (Kobenhavn). 38(4):382-392, 1976.

The effect of 2 weeks' treatment with amylobarbitone, flurazepam, a combination of methaqualone and diphenhydramine, or glutethimide, and their interaction with alcohol, was examined in 40 healthy volunteers in two double-blind cross over trials. Psychomotor skills were tested by a choice reaction test, two coordination tests and a divided attention task 30, 90 and 150 minutes after the previous administration of alcohol or placebo. After both trials were over the subjects of the latter trial were tested once more after one night's deprivation of sleep. Amylobarbitone and flurazepam alone impaired eye/hand coordination whereas the residual effect after methaqualone and diphenhydramine or glutethimide on psychomotor performance was negligible. Amylobarbitone and flurazepam also enhanced the alcohol induced impairment of coordinative skills. Deprivation of sleep did not impair psychomotor performance. The subjects regarded flurazepam and the combination of methaqualone and diphenhydramine as more potent hypnotics than glutethimide or amylobarbitone. Flurazepam and the combination caused most of the side-effects reported by the subjects. 15 references. (Author abstract)

241425 Bech, P. Psychochemistry Institute, Rigshospitalet 9, Blegdamsvej DK-2100 Copenhagen, Denmark **Mental illness and simulated driving: before and during treatment.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 8(4):143-150, 1975.

By use of a car simulator, the driving behavior of 46 psychiatric inpatients was tested before and during treatment. On the basis of the presence of psychotic symptoms, the patients were divided into a psychotic and a nonpsychotic group and matched according to age, sex, and driving experience. Before treatment the psychotic group had a statistically significant prolongation of brake time, and their performance deteriorated more markedly over trials. During treatment there was no statistically significant difference between the two groups. It is indicated that antipsychotic drugs given to psychotic patients do not impair their driving, but do increase their vigilance. 14 references. (Author abstract)

241736 Eckmann, F.; Immich, H.; Scheurlen, H. R. Landeskrankenhaus Stadtfeld, 238 Schleswig, Germany **/Are neuroleptic drugs anticarcinogenic?/** Konnen Neuroleptika Krebs verhuten? Pharmakopsychiatrie Neuro-psychopharmakologie (Stuttgart). 8(6):357-365, 1975.

Statistics are cited which support the theory that a connection exists between the administration of neuroleptic drugs and a lower cancer mortality rate. An epidemiological survey of relative risk in 232 matched groups of patients suggests that patients under neuroleptic treatment had approximately half the risk of dying of cancer as the controls. However, further analysis shows the neuroleptic group and the controls represent two distinct populations which cannot be compared. 5 references. (Journal abstract modified)

241763 Schappi, Rolf; Dick, Pierre Cours de Rive 3, CH-1204, Geneva, Switzerland **/On hypotension as a result of psychotropic medication: comparative study of two correctives (Etilefrine and dihydroergotamine)./** A propos de l'hypotension consecutive aux medicaments psychotropes: etude comparative de deux medicaments correcteurs (Etilefrine et dihydroergotamine). Therapeutische Umschau (Revue Therapeutique) (Bern). 32(8):515-519, 1975.

In a double-blind cross-over clinical trial, the effects of 2 weeks' treatment with Etilefrine or dihydroergotamine on hypotension resulting from psychotropic therapy were compared. Although none of the differences between pretreatment and posttreatment values or between the two drugs attained statistical significance dihydroergotamine appeared to have a more beneficial effect on the subjective symptoms. Blood pressure values showed virtually no changes. In the light of these results, the methodology of this type of drug trial is criticized. 13 references. (Journal abstract modified)

241765 Dick, P. Clinique psychiatrique de Bel-Air, CH-1225 Chene-Bourg/Geneva, Switzerland **/Secondary effects of lithium treatment. Preliminary results of an inquiry./** Les effets secondadres des traitements au lithium (premiers resultats d'une enquete). Therapeutische Umschau (Revue Therapeutique) (Bern). 32(8):532-535, 1975.

Unwanted side-effects occasionally occur either initially or at a later stage in cases of treatment with lithium. Their incidence was evaluated in 146 patients having undergone 182 courses of treatment lasting from 1 to 6 years in most cases. A comparison was made between the various available lithium salts. The incidence of side-effects was found to be markedly higher with lithium carbonate than with lithium sulfate. With lithium sulfate the blood lithium levels remained within a narrow range during the 12 hour period following administration, thus affording a more precise control of the treatment and a simplified therapeutic schedule. 19 references. (Journal abstract modified)

241900 Paulson, George W. Division of Neurology, Department of Medicine, Ohio State University, Columbus, OH 43210 **Tardive dyskinesia.** Annual Review of Medicine. 26:75-81, 1975.

Tardive dyskinesia (TD) is described as a well defined neurologic entity and a major iatrogenic disease. Historical acceptance of the phenomenon is reviewed along with the clinical features. Further details are offered on neuropharmacology of TD, pathology, therapy, and philosophical aspects, and some remaining questions are noted. It is concluded that the treatment consists of prevention by cautious use of phenothiazines, and symptomatic management of intractable cases. The prolonged application of phenothiazines is particularly hazardous for the aged, the very young, and brain-

damaged patients, in whom it may produce tardive dyskinesia. Interruption of phenothiazine therapy or medication programs with methylphenidate, methysergide maleate, some anticonvulsants and other drugs with correlative effect should be considered. Awareness by the internist is mandatory, not only to avoid misdiagnosis and legal complications, but also to avoid worsening of the condition. 9 references.

241990 Denckla, Martha Bridge; Bemporad, Jules R.; MacKay, Mary C. 710 West 168th Street, New York, NY 10032 **Tics following methylphenidate administration: a report of 20 cases.** Journal of the American Medical Association. 235(13):1349-1351, 1976.

Twenty children who developed tics or whose previously existing tics were exacerbated following methylphenidate hydrochloride administration are discussed. Tics developed in 14 children and tics became worse in the other six children. The clinical diagnosis in 19 cases was minimal brain dysfunction, and in one case, Gilles de la Tourette syndrome. Duration and dose of medication showed no particular pattern. In only one case did tics persist unchanged after methylphenidate treatment was discontinued. Tics related to methylphenidate administration appear to be rare (20 of 1520 cases) and may point to a specific susceptibility possibly related to personality profile (e.g.,obsessive, perseverative, withdrawn). 11 references. (Author abstract modified)

242267 Lamb, P.; Mindham, R. H. S.; Ezzat, M. A. Professorial Unit, Mapperley Hospital, Nottingham, NG3, 6AA, England **Parkinsonism induced by fluphenazine decanoate.** Lancet (London). No. 7957:484, 1976.

Six schizophrenic patients whose symptoms are controlled by injections of fluphenazine decanoate every 4 weeks were studed for a total of 26 months to determine the course of drug induced parkinsonism. Observations suggest that the signs are most severe in the third week after the injection. Although the severity of the signs varied from month to month, a general pattern emerged. There is no evidence of a practice effect or of a gradual decline in severity. Data are discussed in terms of prior belief that extrapyramidal signs are at their worst 3-5 days after injection, and that antiparkinsonism drugs may be needed during this period only.

16 METHODS DEVELOPMENT

241777 Lopez, J. B.; Buttery, J. E. Division of Biochemistry, Institute for Medical Research, Kuala Lumpur, Malaysia **Serum lithium measurement of the EEL flamephotometer.** Modern Medicine of Asia (Hong Kong) 11(7):17-18, 1975.

The measurement of serum lithium on a flamephotometer was investigated. Appropriate blanks, pooled serum, standard solution and test serum diluted five fold with 20% (volume/volume) acetone are aspirated. Quantitation is by the Beer's law as the instrument gives a linear response for lithium up to 4 mmol/liter. Results by the proposed method and another flame emission method compared very well ($r = 0.99$). Control sera assayed by the proposed method also gave good agreement with the manufacturer's values. The between batch precision for the method is acceptable. 6 references. (Author abstract)

17 MISCELLANEOUS

239298 Scheff, T. J. University of California, Santa Barbara, CA **Medical dominance: psychoactive drugs and mental health policy.** American Behavioral Scientist. 19(3):299-317, 1976.

Present laws which establish medical dominance in the mental health field are criticized as costly and unwise. It is stated that these laws encourage treatment policies and practices which overemphasize chemotherapy and underemphasize sociopsychological treatment. Some of the scientific evidence relevant to these policies and practices is reviewed. Suggestions are made for alternative policies and for research projects which could provide support for legislative change. 26 references. (Author abstract modified)

239607 Lecrubier, Y.; Widlocher, D. no address **/Acute confusional states./** Les etats confusionnels aigus. Revue de Gerontologie d'Expression Francaise (Paris). No. 6:21-22, 1975.

Treatment of acute confusional states in the elderly is discussed. Such treatment should take place in the hospital; treatment personnel should be as stable as possible. Neuroleptic drugs are often effective with this syndrome, but can sometimes involve the recrudescence of some symptoms. Levomepromazine or thioridazine, effective with agitation, are sometimes contraindicated because of their effect on the autonomous central nervous system. The butyrophenones are thus better indicated. Pimozide or clothiapine or droperidol are effective and have few extrapyramidal effects. When no organic origin of the syndrome can be found, etiological treatment can only begin after restoration of a normal mental state. An extensive somatic examination is necessary, together with an evaluation of vigilance, memory, attention, and complex behavior. With respect to long-term psychotherapy, the therapist must be aware of the negative countertransference which often occurs in treating the elderly.

239678 Davis, J. M. Dept. of Psychiatry, Univ. of Chicago, Chicago, IL **Clinical pharmacology and the prescription of psychotropic medication.** Pharmakopsychiatrie Neuro-psychopharmakologie (Stuttgart). 8(6):332-339, 1975.

Cost data and the pharmacokinetics of psychotropic drugs are illustrated, and a basis for determining adequate pill size for unit dosage is suggested. It is noted that on a cost per milligram basis, there is economic savings if medication is prescribed in the largest size the patient can conveniently take. Pharmacological data support a rationale for higher unit dosage. They indicate a dose response relationship between dose and therapeutic effectiveness and probably a blood level relationship. The long half-life indicates that once a day medication is a reasonable dosage schedule. The most important evidence for once a day medication, however, is the empirical evidence that it works and is safe. Dosage information from double-blind investigations provides a basis for determining adequacy of pill size for antipsychotic therapy. 19 references. (Author abstract modified)

239679 Burrell, C. D. Sankoz Inc., East Hanover, NJ 07936 **Higher unit dosage of psychotropic drugs.** Pharmakopsychiatrie Neuro-psychopharmakologie (Stuttgart). 8(6):340-345, 1975.

An overview of arguments for and against higher unit dosage of psychotropic drugs are presented. It is noted that the realities of the marketplace dictate that pharmaceutical companies seek to develop higher unit dosage forms and that technical problems frequently hinder such development. In low doses once a day medication with psychotropics is possible and practical. The potential for adverse reactions frequently renders it desirable to divide higher daily doses into two separate doses, one given in the morning and the other in the evening. 16 references. (Author abstract)

239680 Scoville, B. Bureau of Drugs, FDA, Washington, DC **Higher unit dosage of psychotropic drugs.** Pharmakopsychiatrie Neuro-psychopharmakologie (Stuttgart). 8(6):345-347, 1975.

A number of problems in recommending specific changes in conventional dosage regimens are outlined. It is suggested that a major reason for reluctance to adopt new regimens using less frequent dosing is the relative paucity of data demonstrating that less frequent, higher dosing is as effective as conventional regimens. Intrinsic methodological and pharmacological problems make it difficult to generate such data for psychotropic drugs. Nonetheless, recommendations for less frequent, higher, psychotropic dosage regimens will become more common in package inserts. (Author abstract)

239681 Abuzzahab, F. S. Dept. of Psychiatry, Univ. of Minnesota, Minneapolis, MN **Obstacles in implementation of higher unit dosage of psychotropics drugs.** Pharmakopsychiatrie Neuro-psychopharmakologie (Stuttgart). 8(6):348-351, 1975.

Obstacles in implementation of higher unit dosage of psychotropic drugs are discussed. It is noted that practitioners, nurses, pharmacists and patients themselves must be considered in a discussion of higher unit dosage of psychotropic medication. Physicians need postgraduate education to overcome their reluctance to prescribe higher unit dosages, and nurses need inservice training regarding principles in clinical pharmacology to comply with changing prescribing practices. Higher unit dosage also leads to less medication error and frees considerable nursing time. Pharmacists face a problem in inventory costs, therefore are reluctant to stock a variety of dosages. Patients taking multiple medications in high dosages hesitate to take large numbers of low dosage pills, thus patient compliance is enhanced with higher unit dosage. It is concluded that blood level data on formulations of higher unit dosage should be the basis of FDA considerations, rather than treating a higher unit dosage as a new drug, and that the final responsibility in providing higher unit dosage rests with the pharmaceutical companies. However, the introduction of higher unit dosage should not be used as a justification to increase cost per milligram of the same medication. 16 references. (Author abstract modified)

239768 Wieck, H. H. Universitats-Nervenklinik, Schwabachanlage 10, 852 Erlangen, Germany **/Psychopharmaceuticals in the hands of the general practitioners -- vertigo states: overview and short reports./** Psychopharmaka in der Hand des Allgemeinarztes -- Schwindelzustande: Ubersicht und Kurzreferate. Medizinische Welt (Stuttgart). 26(13):614-627, 1975.

A collection of reports on psychopharmaceutical treatment in general medical practice is presented. Topics covered included the present use of psychopharmaceuticals in general practice, the diagnosis and treatment of vertigo states, the pharmacology of psychopharmaceuticals, psychiatric symptoms and their pharmaceutical indications, the therapy of manic-depressive diseases, the psychopharmacotherapy of acute schizophrenia, long-term treatment of schizophrenia, the

neurological and psychiatric side-effects of psychopharmaceuticals, the treatment of psychovegetative syndromes, psychopharmaceuticals and psychotherapy, and the geriatric use of psychopharmaceuticals. 15 references.

239846 no author. no address **Evaluation of psychotropic drugs: a symposium.** Inpharma (Hong Kong). No. 23:16-17, 1976.

Highlights of a symposium on the evaluation of psychotropic drugs held in May 1974 are presented. Topics discussed include: 1) some difficulties in interpreting plasma level studies; 2) the value of sleep research as a method for studying psychotropic agents; 3) the desirability of considering work performance in evaluation and selection of psychotropic drugs; and 4) drawbacks of the double-blind placebo controlled trial in assessing drugs in schizophrenia.

240086 Silverstone, T.; Turner, P. no address **Drug treatment in psychiatry.** London, Routledge & Kegan Paul, 1974. 223 p. L4.00.

Aspects of drug treatment in psychiatry are summarized. A historical survey and grouping of psychopharmacological drugs is presented, followed by chapters on pharmacology and methods of examination of the central nervous system. Clinical practice is discussed, and descriptions are offered of the psychiatric diseases for which the drugs are used. Preparation indexes are also presented.

240278 Winstead, Daniel K.; Lawson, T.; Abbott, D. Neuropsychiawtric Clinic, US Army Hospital, Nuremberg, Germany, APO New York, NY 09696 **Diazepam use in military sick call.** Military Medicine. 141(3):180-181, 1976.

The underlying psychologial factors of those patients prescribed diazepam in a general medical outpatient setting (military sick call) were evaluated and compared with appropriate controls. The hypothesis that the popularity of diazepam is due to its use in treating the many manifestations of anxiety as seen in virtually every medical and psychiatric diagnostic category was confirmed by the Minnesota Multiphasic Personality Inventory (MMPI) results. The MMPI results showed that the diazepam group was more anxious and more apt to somatize their difficulties. It is suggested that while diazepam is initially an effective medication in the treatment of these difficult patients, further counseling or psychiatric consultation may be required in their long-term management. 6 references.

240444 Pichot, Pierre. Hopital Sainte Anne, 100 Rue de la Sante, F-75014 Paris, France **/Methodology of therapeutic effectiveness trials in psychopharmacology./** Methodik der Effizienzprufung in der Psychopharmakologie. Archiv fur Psychiatrie und Nervenkrankheiten (Berlin). 220(4):281-288, 1975.

General methodological aspects of therapeutic effectiveness trials in clinical psychopharmacology are discussed under three main categories: the definition of the concept of disease, treatment, and observations of improvement. The main difficulties encountered in such research are illustrated with concrete examples. It is concluded that in spite of the methodological problems, the cost of using adequate experimental designs is more than balanced by the reliability of the resulting statistical conclusions. 7 references. (Author abstract)

240522 White, James H. Adolescent Inpatient Unit, Univ. of Texas Medical Branch, Div. of Child and Adolescent Psychiatry, Galveston, TX **The use and misuse of psychotropic drugs in children.** Psychiatry Digest. 37(2):13-16, 1976.

Arguments for and against the use of psychotropic drugs with children are presented. The importance of psychopharmacologic agents in the total therapeutic plan is stressed, and the use of pharmacologic therapy in the modification of certain target symptoms which have been specifically identified is discussed. Specific treatment of the following seven target symptoms is described: hyperkinesis, enuresis, night terrors and sleepwalking, childhood psychosis, Gilles de la Tourette's syndrome, and insomnia. Possible reasons for inapproapriate use or misuse of psychotropic drugs in children are suggested. It is concluded that, if specific indications and limitations are observed in the use of psychopharmacologic therapy in children, and specific target symptoms are selected and the drug chosen to treat that particular symptom, then pharmacologic therapy should be successful in the majority of patients and many of the problems involving the use of psychoactive drugs may be avoided.

240599 Weithorn, Corinne J.; Ross, Roslyn. School of Education, Queens College, Kissena Blvd., Flushing, NY 11367 **Stimulant drugs for hyperactivity: some additional disturbing questions.** American Journal of Orthopsychiatry. 46(1):168-173, 1976.

Continued professional recognition and concern are urged in regard to increased use of stimulant drugs for treatment of hyperactivity in children. It is contended that drug therapy should be accompanied by adequate interdisciplinary communication about specific behaviors leading to referral and treatment and adequate assessment of the behavioral and educational consequences of medication. A review of the literature is presented, and pertinent questions are posed. 22 references. (Journal abstract)

240614 Snyder, Bruce D.; Harris, Sandra. Dept. of Neurology, St. Paul-Ramsey Hospital and Medical Center, 640 Jackson St., St. Paul, MN 55101 **Treatable aspects of the dementia syndrome.** Journal of the American Geriatrics Society. 24(4):179-184, 1976.

Several case studies are presented to demonstrate that, with attentive medical management, the elderly demented patient can live in greater comfort, dignity and independence than is often the case. Errors in supervision can result in drug intoxication, misdiagnoses, and personal neglect. Many of the elderly have a chronic dementing illness and disability often is accelerated by complications; however, some of these complications are treatable. Pitfalls in the care of such patients are discussed. Treatment involves the correct choice and proper administration of psychotropic drugs. 20 references. (Author abstract)

240704 Mutschler, E. Pharmakologie fur Naturwissenschaftler, 6 Frankfurt/Main, Robert-Mayer-Str. 7, Germany **/Pharmacology of psychoactive drugs./** Pharmakologie der Psychopharmaka. Medizinische Welt (Stuttgart). 26(25):1211-1214, 1975.

Information on the efficiency mechanisms of psychoactive drugs is presented. The drugs are classified into several groups: neuroleptic drugs; antidepressant drugs, such as the thymoleptic drugs; tranquilizers; and psychodysleptic drugs. The range of indications and contraindications, the chemical compounds and concomitant symptoms are explained in detail for each group.

240705 Hippius, H.; Meyendorf, R. Psychiatrische Universitats Klinik, 8 Munich 2, Nussbaumstr. 7, Germany **/General principles of psychopharmacology./** Allgemeine Richtlinien fur

den Einsatz der Psychopharmaka. Medizinische Welt (Stuttgart). 25(26):1215e1220, 1975.

General guidelines for psychopharmacological therapy are presented. The basic requirement for treatment is felt to be a full knowledge of the drug and its indications before implementation of therapy. The psychoactive drugs are grouped into antidepressants, neuroleptics and tranquilizers. Indications, contraindications, concomitant symptoms and complications are outlined for each group. Problems of drug selection from the physician's viewpoint, particularly in regard to endogenous and symptomatic psychoses, neuroses and psychopathies, are explained. A detailed description of variables is presented, including dosage, duration, side-effects and therapy control. 1 reference.

240706 Leutner, Victor. 7889 Grenzach-Wyhlen, Gipshalden 8, Germany /**Efficiency profiles of tranquilizers and broad spectrum psychosomatic drugs.**/ Zum Wirkungsprofil der Tranquilizer und Breitband-Psychosomatika. Medizinische Welt (Stuttgart). 26(25):1221-1224, 1975.

The efficiency mechanisms of various tranquilizers and broad spectrum psychosomatic medicines available in Germany are classified. The evaluation of charts and tables in regard to psychosedation and analgesia is emphasized. Satisfactory results are outlined for chlordiazepoxide, amitriptyline, and an antidepressant and analgetic drug as well. The problem of the median lethal dose and the danger of suicide is briefly discussed. 13 references.

240708 Kohlmeyer, Knut. 63 Giessen, Am Steg 22, Germany /**Psychopharmacological drugs in neurology.**/ Psychopharmaka in der Neurologie. Medizinische Welt (Stuttgart). 26(25):1230-1233, 1975.

The use and efficiency mechanisms of psychoactive drugs in neurology are discussed. Their influences on the ascending and the descending reticular systems are explained. It is noted that despite the almost limitless number of psychopharmacological drugs, only a few are applicable in neurology. Examples of use of psychoactive drugs and their indications are explained for several conditions: epilepsy, apoplexia, subarachnoid hemorrhage, pyramidal spasticity, muscular atrophies, trigeminal neuralgia, lumbago, myasthenia gravis, and pseudoparalytica.

240723 Windorfer, A. 7800 Freiburg/Brsg., Mathildenstr. 1, Germany /**New developments in the use of phenobarbital in pediatrics.**/ Neue Anwendungsmoglichkeiten fur Phenobarbital in der Padiatrie. Medizinische Welt (Stuttgart). 26(35):1524-1526, 1975.

New developments in the use of phenobarbital (Luminal) in pediatrics are reported. It was found that the microsomal enzyme system is stimulated by 300-500% through administration of the drug. The decreasing effect for the bilirubin level is described in the case of newborns of mothers who have taken the drug shortly before birth. Its ambiguous effects in regard to a prophylactic for hyperbilirubinemia are outlined. Results show the drug to be effective with respect to the Crigler-Najjar syndrome, the Gilbert-Meulengracht syndrome, and spasmodic diseases.

240838 Moizeszowicz, Julio. Hospital Nacional Neuropsiquiatrico "Jose T. Borda", Servicio No. 26, Buenos Aires, Argentina /**A primer on the clinical evaluation of psychotropic drugs.**/ Actualizacion en la evaluacion clinica de psicofarmacos. Acta Psiquiatrica y Psicologica de America Latina (Buenos Aires). 21(1):41-51, 1975.

Different research concepts and designs used in the clinical evaluation of psychotropic drugs are analyzed. The need for universally accepted rating scales for the purpose of evaluating clinical effects is emphasized. Several rating scales are reviewed, and the usefulness of nonparametric statistical techniques is compared to that of parametric techniques. Dangers inherent in generalizing from one population to another are noted. It is recommended that the physician limit his use of rating scales to self-evaluation scales used by the patients. 26 references. (Journal abstract modified)

241240 Goldstein, Dora B. Dept. of Pharmacology, Stanford Univ. School of Medicine, Stanford, CA 94305 **Pharmacological aspects of physical dependence on ethanol.** Life Sciences (Oxford). 18(6):553-561, 1976.

The application of pharmacological concepts, such as dose responses, time courses, drug interactions and pharmacogenetics, to the study of physical dependence on ethanol is reviewed. Experimental establishment of physical dependence in animals is discussed. It is noted that dependence develops rapidly, that it is related to the cumulative alcohol dose, and that the rate of recovery from dependence is also rapid. Possible mechanisms of biochemical changes are outlined, and the roles of neurotransmitters, adrenal steroids, acetaldehyde, and adenosine triphosphatase are reviewed. The use of animal models to test drugs for possible therapeutic use in human abstinence syndromes is suggested, and genetic modification of withdrawal reactions is described. Implications of findings for the theory that drug addiction is an adaptive process are discussed. 77 references.

241435 Llinas, Jose J. 3615 S. W. 13th St., Gainesville, FL 32608 **Early strategies in treatment of the depressed patient.** Journal of the Florida Medical Association. 63(4):271-276, 1976.

It is asserted that management of most depressed patients is well within the capability of the family physician. It is suggested that family physicians upgrade or develop skills in four basic areas: 1) engaging the patient in a trusting relationship; 2) appraising lethality in suicidal crisis; 3) using antidepressant medication correctly; and 4) being aware of the psychiatric resources within his own community, for those patients he cannot or will not treat himself. A brief overview of the symptomatology of depression is presented, and insights into the nature of self-blame and the personality traits of depressives are offered. The pharmacological approach to treating depression is outlined. 12 references. (Author abstract modified)

241471 Romero, Jorge A. Dept. of Neurology, Massachusetts General Hospital, Boston, MA 02114 **Influence of diurnal cycles on biochemical parameters of drug sensitivity: the pineal gland as a model.** Federation Proceedings. 35(5):1157-1161, 1976.

Diurnal cycles in physical parameters in the environment which modulate biochemical and physiological circadian rhythms in experimental animals are discussed, with reference to studies of the rat pineal gland as a model for changes in drug sensitivity. It is noted that environmental lighting synchronizes cycles of indole metabolism and melatonin synthesis in the rat pineal gland by modulating the activity of postganglionic sympathetic nerves: as a result, the sensitivity of pineal N-acetyltransferase to stimulation by isoproterenol or by dibutyryl cyclic adenosine-3',5'-monophosphate (AMP) varies diurnally. Cycles in sensitivity to isoproterenol reflect cycles in the system that regulates cyclic AMP production, and include variations in the availability of specific beta-adrenergic

binding sites and in the sensitivity of receptor coupled adenylate cyclase to enzymes. The effects of diurnal cycles of environmental lighting on other systems are considered. 38 references. (Author abstract modified)

241472 Fernstrom, John D. Laboratory of Brain and Metabolism, Dept. of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **The effect of nutritional factors on brain amino acid levels and monoamine synthesis.** Federation Proceedings. 35(5):1151-1156, 1976.

Evidence that acute dietary manipulations can modify the synthesis of serotonin and catecholamines in the brain is reviewed, and data indicating that diet can substantially modify biochemical actions of centrally acting drugs are presented. Studies are reported which demonstrate that the ingestion of single meals can rapidly modify the levels and synthesis of brain monoamine neurotransmitters. The physiological control of serotonin synthesis by tryptophan availability and of catecholamine synthesis by tyrosine availability is described. Suggestions are made for controlling food intake during the course of pharmacological experiments, to eliminate unwanted effects of food ingestion on brain monoamines. 26 references.

241753 Adam, Kirstine; Adamson, Liisi, Brezinova, Vlasta; Oswald Ian. University Department of Psychiatry, Royal Edinburgh Hospital, Edinburgh EH10 5HF, England **Do placebos alter sleep?** British Medical Journal (London). 1(6003):195-196, 1976.

Ten volunteers, six women and four men, aged 41 to 62 years old (representing the age and sex distribution of patients who most often complain of inadequate sleep) were given placebos with a written statement that the pill was a mild sleeping pill which would help to make their sleep more restful without causing any hangover. It was found that the suggestion that the inert capsule was a sleeping pill did not influence subjective ratings of sleep quality or anxiety or the electrophysiologically recorded features of sleep in the 10 volunteers. 9 references. (Author abstract modified)

241754 Gazzard, B. G.; Davis, M.; Spooner, J.; Williams, Roger. Whipps Cross Hospital, London E11, England **Why do people use paracetamol for suicide?** British Medical Journal (London). 1(6003):212-213, 1976.

A questionnaire to assess motives for choosing paracetamol as a suicide agent was completed by 107 patients admitted to a hospital in England after an overdose of the drug. None of the 48 patients interviewed would have chosen paracetamol had they known that there would be an interval of two to three days before the onset of serious symptoms. Only five of the patients had obtained the drug on prescription, but the remainder had obtained it easily from a retail pharmacy. There was no apparent reason for the preference for paracetamol. It is suggested that it would be difficult to restrict the availability of paracetamol, and that educating the public about the effects of an overdose would be more appropriate. 15 references. (Author abstract)

241870 Braga, Joao Carlos. Disciplina de Psiquiatria, Hospital de Clinicas, Univ. Federal do Parana, Rua General Carneiro, s/n, 80000 Curitiba, Brazil **/Dependency on combined methaqualone-diphenhydramine./** Dependencia pela associacao metaqualona-difenidramina. Arquivos de Neuro-Psiquiatria (Sao Paulo). 33(3):261-267, 1975.

The cases of four patients admitted to a psychiatric hospital for addiction to the combination drug methaqualone/diphenhydramine are reported. The clinical features of the cases and the dependence of the patients on the drug are discussed. All of the patients came from above average social classes; three of them were homosexuals, and the last patient was poorly adjusted in a heterosexual relationship. 21 references. (Journal abstract modified)

241902 Holman, R. Bruce; Elliott, Glen R.; Barchas, Jack D. Lab. of Behavioral Neurochemistry, Dept. of Psychiatry, Stanford University School of Medicine, Stanford, CA 94305 **Neuroregulators and sleep mechanisms.** Annual Review of Medicine 26:499-520, 1975.

Recent neuropharmacological and biochemical data related to hypotheses of the control of sleep by neuroregulators are reviewed. The effects of 5-hydroxytryptamine (5-HT) are discussed in terms of lesions, pharmacological depletion, electrical stimulation, the administratin of 5-HT and related compounds, monoamine oxidase inhibitors, and neurophysiological and neurochemical parameters. Related effects of the catecholamines norepinephrine and dopamine are also examined, along with those of acetylcholine and other possible neuroregulators. It is concluded that the potential for manipulation of sleep is of obvious importance in illnesses such as insomnia, narcolepsy, and sleep apnea, and may also be valuable in the treatment of such conditions as psychosis and depression, where sleep disturbances are an important component of the illness. 248 references.

242265 Warburton, David M. Reading University, England **Brain, behaviour and drugs.** London, Wiley, 1975. 280 p. $15.30.

An introduction to the brain processes which may underlie behavior is presented in a discussion of problems related to biologically oriented psychiatry. Psychopharmacological agents are examined in terms of clinical effects and the actions of drugs as clues to the nature of psychiatric illness.

242269 Anderson, William H.; Kuehnle, John C. Massachusetts General Hospital, Boston, MA **Dosage of antipsychotic drugs.** New England Journal of Medicine. 294(12):670, 1976.

Disagreement is expressed with Baldessarini's suggestion that psychotic patients should be treated with haloperidol up to 15mg for 2-3 months before an increase in dosage. Although it is agreed that exposure to antipsychotic drugs should be the minimum dose and duration possible to achieve and retain remission of symptoms, a contrary strategy is suggested which uses high initial doses. It is argued that, if early remission occurs, the dose can quickly be reduced to a low maintenance level. 5 references.

242720 Harrer, G. Landes-Nervenklinik, Ignaz-Harrer-Strasse 79, A-5020 Salzburg, Austria **/Psychotropic drugs from the practitioner's point of view./** Psychopharmaka aus der Sicht des Praktikers. Wiener Medizinische Wochenschrift (Wien). 124(38):541-546, 1974.

A practical discussion of psychotropic drugs considers the use of neuroleptics, antidepressants, and tranquilizers. Their complicated and unpredictable nature, and the limitation to a few substances since all have similar generic chemical compositions are noted. Representative brands of drugs under the three categories are listed. Four cautionary measures are indicated relative to dosages of highly effective psychotropic drugs: 1) pharmacodynamic effects of psychotropic drugs exhibit considerable interindividual and intraindividual variations;

2) the primary side-effects are dependent on the dosage and vary quantitatively and qualitatively; 3) psychotropic drugs can reinforce the potency of other simultaneously ingested medication; and 4) under normal psychic conditions psychotropic drug impulses are integrated within the personality, but under certain experiential constellations the effect can be canceled out or become contradictory. Tranquilizers are discussed as to type and dosage. Two case illustrations underline the extent of their possible behavioral influence. 4 references.

242744 Coyle, I.; Wayner, M. J.; Singer, G. Swinburne College of Technology, Hawthorn, Victoria, Australia **Behavioral teratogenesis: a critical evaluation.** Pharmacology, Biochemistry and Behavior. 4(2):191-200, 1976.

Some relevant literature concerning the effects of prenatal administration of drugs and several other substances on postnatal behavior is reviewed. Significant variables and problems in the adequate design of experiments to assess these effects are discussed. Although the evidence concerning prenatal drug effects on behavior is equivocal, sufficient data exist to indicate that this will continue to be a viable and important area of research in the future. Present results demonstrate the complexity of drug interactions with other variables. 91 references. (Author abstract)

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